621 Real World Study

STUDY ID

CT LUCIA 621P-BER-401-21

PROTOCOL

Version 1

31-Aug-2022

NCT05646004

ZEISS classification: Restricted

CONFIDENTIAL

Medical Device Clinical Investigation Plan

Protocol number.: CT LUCIA 621P-BER-401-21

Short title: “621 RWS”

An open single-arm clinical investigation to evaluate the clinical safety and effectiveness of CT LUCIA 621P indicated for the visual correction of aphakia secondary to the removal of the crystalline lens in patients with cataracts

Name of test medical device: Intraocular lens

Model and specification: CT LUCIA 621P

Class III medical devices requiring clinical trial approval Yes☐ No☒

Protocol Version No. and Date: Ver 1.0 / August 31, 2022

Clinical investigation institution: Aier Eye Hospital of BoAo Hope City

Principal investigator: [redacted]

Sponsor: Carl Zeiss Meditec AG [redacted]

[redacted]

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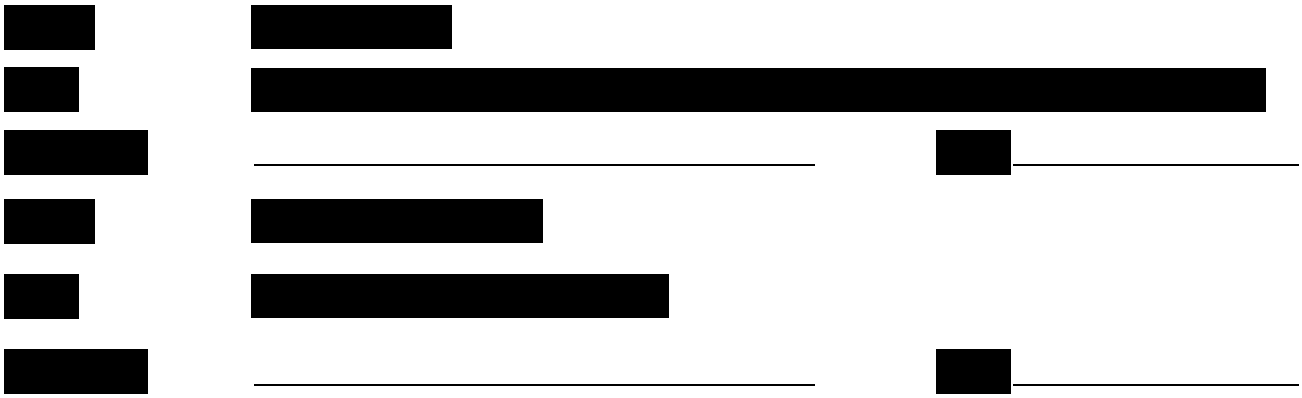
Table 1: CT LUCIA 621P Parameters **17**

2. Revision history

Version	Version date	Reasons reversion	Changes / Justifications
1.0	2022/08/31	Initial issue	NA

3. Approval Form of CIP

This CIP is strictly reviewed and approved by following persons of the sponsor and agent.



4. List of Abbreviations in [redacted] English

Abbreviation	The full name in English	[redacted]
ACD	Anterior Chamber Depth	
AE	Adverse Event	
AL	Axial Length	
c/d	/	
cd/m^2	/	
CDVA	Corrected Distance Visual Acuity	
cm	Centimeter	
CRF	Case Report Form	
DM	Data Manager	
DMP	Data Management Plan	
DVP	Data Validation Plan	
EDC	Electronic Data Capture	
eCRF	electronic Case Report Form	
ETDRS	Early Treatment Diabetic Retinopathy Study	
GCP	Good Clinical Trial Practice	
ICF	Informed Consent Form	
IOL	Intraocular Lens	
IOP	Intraocular Pressure	
LogMAR	/	
m	Meter	
MICS	Micro Incision Cataract Surgery	
mm	Millimeter	
mmHg	Millimeter Mercury Column	
Nd:YAG	Neodymium-doped Yttrium Aluminium Garnet	
NMPA	National Medical Products Administration	
OCT	Optical Coherence Tomography	
PCO	Posterior Capsular Opacification	
SAE	Serious Adverse Event	
SIA	Surgically Induced Astigmatism	
SIOL	Single Focus Intraocular Lens	
SMP	Smooth Micro Phase	
SOP	Standard Operation Procedure	
UDVA	Uncorrected Distance Visual Acuity	
VA	Visual Acuity	

5. Protocol Synopsis

Investigational Device	Intraocular lens
Model	CT LUCIA 621P
Protocol No.	CT LUCIA 621P-BER-401-21
Study Title	An open single-arm clinical investigation to evaluate the clinical safety and effectiveness of CT LUCIA 621P indicated for the visual correction of aphakia secondary to the removal of the crystalline lens in patients with cataracts
Sponsor	Carl Zeiss Meditec AG [redacted]
Working Principle	CZM monofocal IOL CT LUCIA 621P is indicated for the visual correction of aphakia secondary to the removal of the crystalline lens in patients with cataracts. It is sterile, foldable, heparin-coated, hydrophobic, acrylic, monofocal, posterior chamber intraocular lens (IOL) pre-loaded in an injector for implantation in the capsular bag to replace the human crystalline lens.
Planned Sample Size	About 105 Subjects
Plan Duration	From Sep 2022 to Dec 2023
Investigational site	Aier Eye Hospital of BoAo Hope City, [redacted]
Clinical Investigation Design	This clinical investigation is designed as an open, single arm study. After informed consent is signed by the patients and satisfying selection criteria, the patients will be included in the clinical investigation. [redacted] the primary objective of this investigation is to show the effectiveness in regard to the monocular corrected visual acuity (CDVA) of CT LUCIA 621P 6 months after lens implantation. All subjects will be followed up preoperatively, intraoperatively, post-op 1 day, post-op 1 week ± 1 day, post-op 1 month ± 7 days, post-op 3 months ± 14 days, and post-op 6 months ± 30 days. [redacted] Hypothesis that the overall effective rate of the investigational device can reach 92.5% at post-op 6 months, under the condition of a bilateral significance level of 0.05 and a power of 80%,

	[redacted] using the Tests for One Proportion formula in PASS 15 [redacted]  It is calculated that at least 94 patients are required, taking into account a 10% dropout rate, a total of at least 105 patients will be required for this clinical investigation. [redacted]
Inclusion Criteria*	1) Age ≥ 18 years old; 2) Patient with clinically significant cataract with planned phacoemulsification cataract extraction and implantation of CT LUCIA 621P IOL into the capsular bag; 3) Preoperative corneal astigmatism ≤ 1.00D; 4) Patient is willing and capable of providing informed consent; 5) Patient is willing and capable of complying with visits and procedures as defined by this protocol.
Exclusion Criteria*	Subjects who meet any of the following criteria in case screening would be excluded from this clinical investigation: 1) Preoperative best corrected visual acuity > 4.7 or ⩽ 0.3 logMAR; 2) Corneal endothelial cell count less than 2000 cell/mm2; 3) Age under 18 years old; 4) Pregnant and lactating women; 5) Patients who attend other drug or medical device study; 6) Ocular disorder that could potentially cause a clinically significant future visual acuity loss; 7) Anterior segment pathology (e.g. chronic uveitis, iritis, aniridia, rubeosis iridis, anterior membrane dystrophies, poor pupil dilation, etc.) 8) Abnormal corneal finding (e.g. keratoconus, pellucid marginal degeneration, or irregular astigmatism, clinically significant corneal membrane dystrophies); 9) Any condition in the study eye that could affect IOL stability (e.g. pseudo-exfoliation, zonular dialysis, evident zonular weakness or dehiscence, etc; 10) Any acute infection (acute ocular disease, external/internal infection, systemic infection); 11) History of any clinically significant retinal pathology or ocular diagnosis (e.g. diabetic retinopathy, ischemic diseases, macular degeneration, retinal detachment, optic neuropathy, amblyopia, strabismus, microphthalmia, aniridia, epiretinal membrane etc.) in the study eye that could alter or limit final postoperative visual prognosis; 12) Any previous intraocular and corneal surgery ;

	13) Uncontrolled glaucoma or IOP higher than 24mmHg under ocular hypertension treatment; 14) Current systemic or ocular pharmacotherapy that effects patients' vision; 15) Current pathology or condition that could be a risk for the patient according to the investigator opinion; 16) Patients unable to meet the limitations of the protocol or likely of non-cooperation during the clinical investigation; 17) Patients whose freedom is impaired by administrative or legal order. *All eye-related inclusion and exclusion criteria are applicable to the study eye only. If the non-study eye does not fulfil all criteria, the patient can still be enrolled into the study.
Safety Endpoints	**(1) Corneal complications** Type, incidence and frequency (number of events) of corneal complications, such as corneal edema, corneal folds and so on in test eye at postoperative visits; **(2) Corneal endothelial cell count** Corneal endothelial cell counts in test eyes at postoperative visits; **(3) Anterior and posterior segment inflammations** Type, incidence and frequency (number of events) of anterior and posterior segment inflammations in test eyes at postoperative visits, such as buoyant cells of anterior chamber, aqueous flare, hypopyon and the performance of endophthalmitis; **(4) Fundus complications** Type, incidence and frequency (number of events) of fundus complications such as macular edema and retinal detachment in test eyes at postoperative visits; **(5) Intraocular pressure** Intraocular pressure in test eyes at postoperative visits; **(6) Posterior capsular opacification and Nd:YAG capsulotomy** Incidence and frequency (number of events) of posterior capsular opacification and Nd:YAG in test eyes at postoperative visits; **(7) Intraocular lens status** Type, incidence and frequency (number of events) of IOL decentration, tilt, rotation, dislocation, opacity, etc, in test eyes at postoperative visits; **(8) Secondary Surgical Intervention** Incidence of secondary surgical intervention in test eyes at postoperative visits. **(9) Adverse events and serious adverse events** Type, incidence and frequency (number of events) of adverse events and serious adverse events during the clinical trial **(10) Device deficiency** Type, incidence and frequency (number of events) of device deficiency during the clinical trial
Primary Effectiveness Endpoint	Effectiveness rate of product 6 months after implantation. Evaluation criteria: based on the situation of monocular CDVA ≥4.7 (≤0.3 logMAR) at 6 months postoperatively considered as effective, the effectiveness rate is not lower than target value (82.5%).

[redacted]	
Biostatistics	**1) Study Completion and Baseline Description:** ① Description of the completion of the clinical investigation: including the general situation of the clinical investigation (number of subjects screened, number of subjects enrolled, number of subjects who completed the study, number of subjects who lost to follow up / withdrawal / excluded, etc.); ② Baseline description: the baseline demographic indicators, vital signs and other relevant medical history indicators of all the selected subjects (ITT analysis set) shall be described; **2) Effectiveness Evaluation** Effectiveness evaluation: statistical analysis shall be conducted for the full analysis set and per protocol set respectively **3) Safety Evaluation** Adverse events and complications will be recorded directly and possible causes will be analyzed. A list will describe the adverse events and adverse reactions of the treatment group, and gives the causes and explanations. The incidence of person-time adverse events will be calculated, i.e., the incidence of adverse events =100* total number of adverse events for all subjects/total number of cases. All subjects in the group shall be analyzed, and no adverse event shall be missed. At the same time, the specific manifestation, severity, prognosis of all adverse events in each case and the relationship with the study device will be described in detail.

[redacted]

[redacted] / [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
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6. Sponsor information

6.1. Sponsor name

Carl Zeiss Meditec AG [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

7. Institution and principal investigator information

Codename of clinical investigation institutions	The name of the clinical investigation institution	Investigator	Title	Contact details
01	Aier Eye Hospital of BoAo Hope City	[redacted]	[redacted]	[redacted]

8. Justification for the Design of the Clinical Investigation

8.1. Background

A cataract is an opacification of the lens in the eye leading to a decrease in vision. It can affect one or both eyes and often develops slowly. Symptoms may include faded colours, blurry vision, glare and halos around light, trouble with bright lights, and trouble seeing at night. This may result in trouble driving, reading, or recognizing faces [redacted] Poor vision may also result in a decrease in quality of life, an increased risk of falling and depression [redacted]

Cataract is a multifactorial disease associated with age, female sex, genetic predisposition, smoking, diabetes mellitus, drug intake and environmental exposure to UVB radiation [redacted] Cataract is the leading cause of blindness, globally accounting for 33% of the blindness worldwide. Global worldwide prevalence of cataract in adults over 50 years of age was estimated at 47.8% [redacted]

However, the loss of visual function due to cataracts is treatable with modern cataract surgery. During the surgery the clouded lens is removed and replaced by an artificial lens implant (intraocular lens or IOL), which restores vision. New lens designs and materials for artificial intraocular lenses and improvement of surgery technique have greatly reduced the risks of complications during and after cataract surgery. Complications are rare and exchange of the implant is usually not required.

The first IOLs were made of polymethylmethacrylate (PMMA) and implanted by Sir Harold Ridley had noticed to be inert in eyes of World War II aviators struck by flying plastic during combat. With the introduction of phacoemulsification and the possibility to remove the cataract through smaller incisions, foldable materials were developed for IOLs such as hydrophobic acrylic, hydrophilic acrylic and hydrophobic silicone, the three main material groups in use today.

Hydrophilic acrylic lenses are soft, somewhat compressible and show good biocompatibility. Most hydrophilic IOLs are single piece, but these IOLs vary considerably in the shape of their haptics. Hydrophobic acrylic foldable C-loop IOLs were introduced in 1993 [redacted]. They are the most popular worldwide, especially in the US because of FDA approval for Alcon C-loop IOLs. Hydrophilic acrylic IOLs are also often associated with a lower posterior capsule opacification (PCO) and Nd:YAG laser capsulotomy rate [redacted]

The most common type of IOL used in cataract surgery is a monofocal IOL that focuses on one distance point, mostly for clear distance vision. If the surgeon only needs to correct aphakia, a regular (spherical or aspheric) monofocal IOL is the IOL of choice. However, pseudophakic eyes are unable to accommodate and reading glasses or glasses for intermediate distances will be required in addition to an implanted monofocal IOL.

This investigational plan is designed to evaluate the performance of the CT LUCIA 621P, which is a foldable single-piece posterior chamber IOL made with clear Acrylmex™ UV-absorbing hydrophobic acrylic material, with high refractive index (1.489). The CT LUCIA 621P also has heparin surface modification to reduce adherence between the IOL optic and haptic to promote unfolding of the lens after delivery. The use of heparin-coated IOLs has been reported in multiple published studies, none of which report safety concerns beyond those anticipated with the use of traditional IOLs. [redacted]

The monofocal preloaded hydrophobic acrylic intraocular lens CT LUCIA 621P product under study is the third-generation product of Carl Zeiss Meditec AG (hereinafter referred to as Zeiss) CT LUCIA family, the first-generation CT LUCIA 601P and second-generation CT LUCIA 611P is consistent in optical design, product material, surface treatment, optical effective diameter and surgical incision.

8.2. Basic product information

8.2.1. Structure and composition

[redacted]

Table 1: CT LUCIA 621P Parameters

Criteria	CT LUCIA 621P
Manufacturer	Carl Zeiss Meditec AG
Material	Hydrophobic acrylic with heparin coated surface
Haptic design	Modified C Shape haptics, no angulation (zero degrees)
Optic diameter	6.0 mm
Total diameter	13.0 mm
Optical Design	Monofocal, aspheric (aberration correcting)

Criteria	CT LUCIA 621P
Lens design	Single piece
Labeled A-constant	120.2
Dioptric power range	0.0 to +34.0 Diopter (D), in 0.5 D increments
Implantation in	Capsular bag
Incision size	2.2 -2.6 mm
Preloaded Injector (P version)	BLUESERT
Picture	

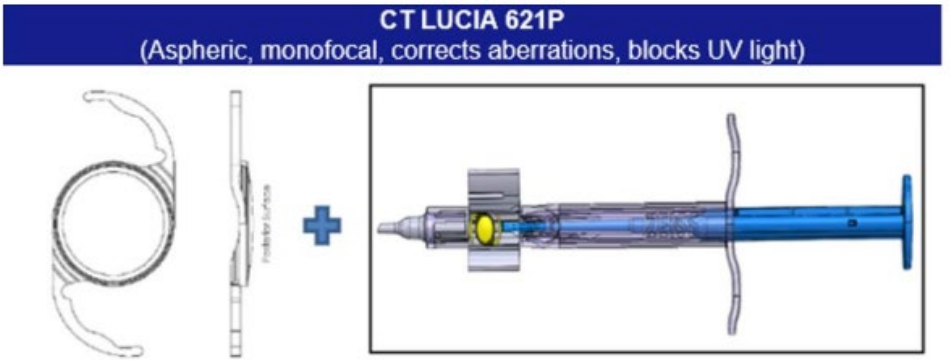


Figure 1: CT LUCIA 621P Structural Composition

The intraocular lens is marked yellow for reader's convenience

The product is colorless and transparent

[redacted]

This product is sterile, foldable, heparin-coated, hydrophobic, acrylic, monofocal, posterior chamber intraocular lens (IOL) pre-loaded in an injector.

8.2.2. Working principle and mechanism

The working principle of the IOL is based on the physical and optical principles of refraction and diffraction of light. The two main properties of hydrophobic monolithic IOLs are:

- Replace the cloudy cataract lens with a clear intraocular lens.
- Light passing through the lens to be focused onto the retina via refraction and diffraction

[redacted]



The most used technique today is the use of a injection system to allow intraocular lenses to be safely and less invasively implanted in a patient's eye. Therefore, typically, physicians need to combine the IOL with a suitable injector and load the IOL into the injector loading chamber. These steps should be performed in accordance with the operating instructions, improper operation may affect the final safety and efficacy.

However, for CT LUCIA 621P, the intraocular lens is completely preloaded, which means that the intraocular lens itself has been placed in the loading chamber of the injector. Its advantage is that doctors do not need to install the intraocular lens into the injector, thus reducing the influence of improper operation on safety and effectiveness. Generally speaking, CT LUCIA series is a fully preloaded one-piece intraocular lens. Injector can make the surgical implantation of foldable hydrophobic intraocular lens more convenient and safer.

[redacted]

[redacted]

8.3. Application scope and related information

8.3.1. Intended use

The intraocular lens CT LUCIA 621P is intended for implantation in the capsular bag to replace the human crystalline lens.

8.3.2. Indication

The intraocular lens CT LUCIA 621P is used for the visual correction of aphakia secondary to the removal of the crystalline lens in patients with cataracts.

8.3.3. Target population

Aphakic adult patients (18 years old or older).

[redacted]

8.3.4. End user

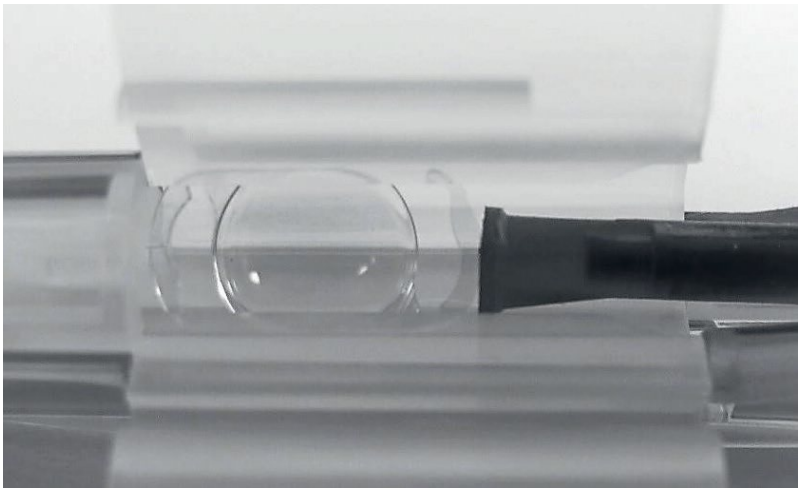
The intraocular lens CT LUCIA 621P shall be handled by health professionals and implanted by physicians.

8.3.5. Use method

Preparatory steps

- Check the label on the lens box to ensure that you have the correct lens model and dioptric power, and that the product is not past its expiration date.
- The use of viscoelastic is required. For best performance, use ZEISS ophthalmic viscoelastic devices (OVDs) and ensure that both the OVD and the pre-loaded instrument have a temperature of at least 18 °C (64.4 °F) during use. The use of balanced salt solution alone is not recommended.
- Remove the tray from the box outside the sterile area. Remove the tray lid in the sterile area and then remove the pre-loaded ZEISS injector from the tray.
- Check the lens is centered and fixed properly in the IOL loading chamber (Figure 4)

Figure 4: Lens in the IOL chamber



- Cover the whole lens and blue plunger head with a large amount of ophthalmic viscoelastic agent (Figure 5). Avoid contact with lens and blue plunger head.

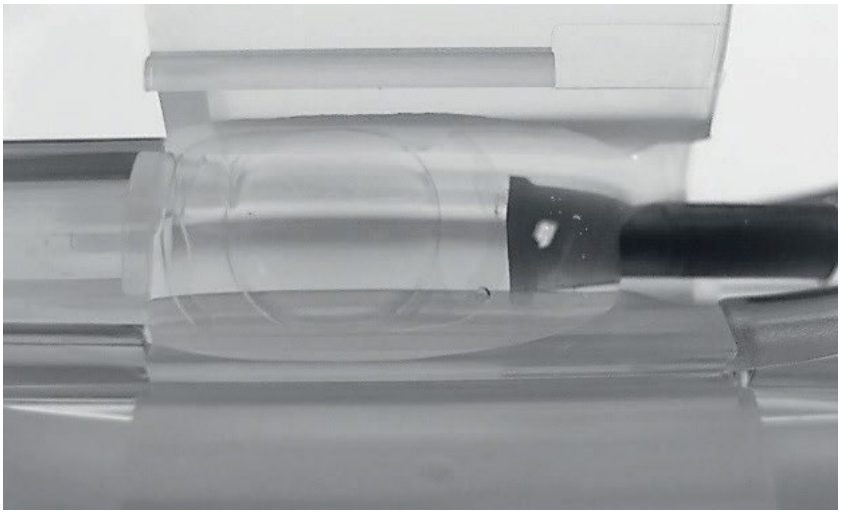


Figure 5: OVD coverage area (rectangle)

- Close the lid of the IOL loading chamber tightly (Figure 6).



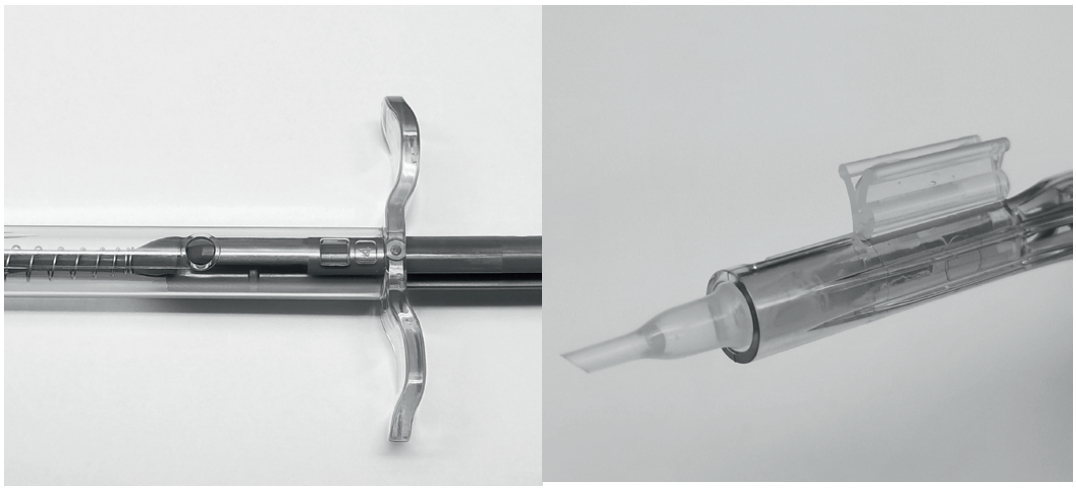
Figure 6: Closed lid of the IOL chamber

IMPORTANT: Allow the lens to remain in this position until the surgeon is ready to implant it into the eye.

Implantation steps

- Advance the lens to the intermediate position. Gently press the plunger forward until an audible “click” is heard (Figures 7 and 8).

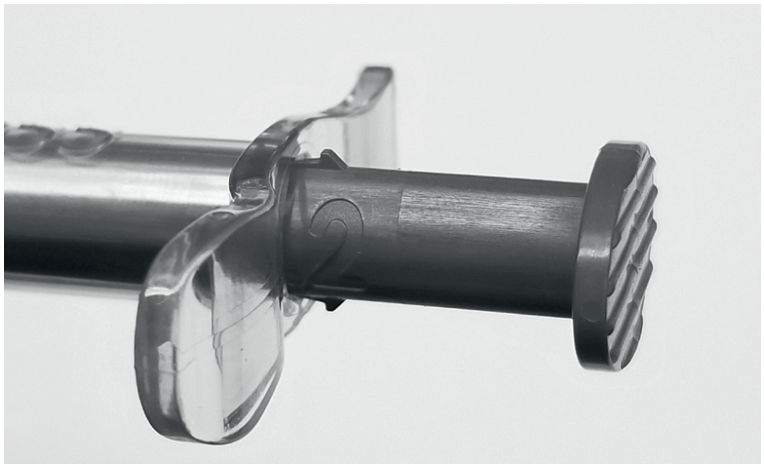
Figure 7 and Figure 8: Lens intermediate positioning



IMPORTANT: The lens should be implanted immediately.

- Injection: loading chamber wings facing upwards. Slowly advance the lens until it has been released from the injector. If delivery is incomplete, apply additional force to the thumb flange to release the lens (Figure 9)

Figure 9: Ramp stop and thumbflange



- Before implantation, please check whether the orientation of IOL is correct:

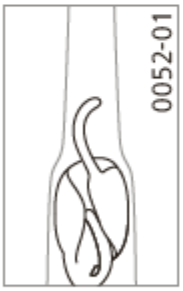
Drawing	Possible haptic configuration	Possible IOL behavior	Recommendation
	Both haptics are tucked into the optic (ideal scenario).	Correct position (no risk).	Proceed.
	Plunger overriding trailing haptic.	The haptic could become pinned between the cartridge and the plunger cushion and the IOL could become stuck in the injector tip. There is a risk that the haptic might tear.	Do not proceed.
	Leading haptic twisted.	The leading haptic may become twisted and may point downward and/or to the right; the optic may begin to roll counter-clockwise and even roll upside down.	Rotate the injector clockwise (bevel to the left) to ensure that the leading haptic is correctly positioned in the capsular bag and proceed as normal.
	Leading haptic is looped but not over the optic.	Haptic can swing out and is slightly off-axis but pointing in the correct direction.	Proceed.

Figure 10: Troubleshooting for correct lens positioning.

- Carefully place the lens in the capsular bag
- Discard the device. Do not reuse the injector.

8.3.6. Warnings, adverse reactions and potential risks

[redacted]

Possible complications linked to surgery for crystalline lens removal and intraocular lens implantation include, but are not limited to, those listed below:

- inflammatory reaction (e.g. vitritis, iritis, iridocyclitis, hypopyon, cyclitic membrane)
- ocular infection (endophthalmitis, microbial keratitis)
- toxic anterior segment syndrome
- wound leakage
- iris prolapse
- pupillary block
- elevated intraocular pressure (IOP) requiring treatment
- corneal edema
- corneal endothelial damage
- retinal detachment
- cystoid macular edema

Potential complications associated with intraocular lenses include:

- secondary cataract
- decentration of the lens
- deviation from target refraction

8.3.7. Precautions

The safety and effectiveness of the IOLs have not been demonstrated in patients with the following pre-existing ocular conditions and intraoperative complications listed below. Careful pre- and perioperative evaluation and sound clinical judgment should be used by the surgeon to determine the risk/benefit ratio before implanting a lens in a patient with one or more of the conditions below:

- perioperative complications (such as posterior capsule rupture, zonular damage, vitreous loss, significant anterior chamber bleeding, or choroidal hemorrhage)
- uncontrolled positive intraocular pressure or glaucoma
- aniridia
- microphthalmos or macrophthalmos

9. Study purpose

To evaluate the clinical safety and effectiveness of CT LUCIA 621P indicated for the visual correction of aphakia secondary to the removal of the crystalline lens in patients with cataracts.

10. Study design

10.1. Overall design and determination criteria

This clinical investigation was designed as an open-label, one-arm study.
Aier Eye Hospital of BoAo Hope City was selected as a clinical research center to carry out this clinical investigation, and after obtaining the patient's informed consent and meeting the selection criteria, the patient will be included in the clinical investigation.

The primary objective of this investigation is to show the effectiveness in regard to the monocular corrected visual acuity (CDVA) of CT LUCIA 621P 6 months after lens implantation. All subjects were followed up preoperatively, intraoperatively, postoperatively for 1 day, 1 week± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days.

[redacted]

Assuming that the overall effective rate of the study device 6 months after surgery can reach 92.5%, the Tests for One Proportion formula in PASS 15 [redacted] will be used with reference to the tests for One Proportion formula in the Principles of Clinical Trial Design Indicators for Medical Devices with a bilateral significance level of 0.05 and a power of 80%.

[redacted]

It was calculated that at least 94 patients were required, taking into account a 10% drop-out rate, for a total of at least 105 patients.

[redacted]

10.2. Subject selection

All eye-related inclusion and exclusion criteria are applicable to the study eye only. If the non-study eye does not fulfil all criteria, the patient can still be enrolled into the study.

10.2.1. Inclusion criteria

Subjects must meet the following inclusion criteria and none of the later exclusion criteria to be enrolled in this study as subjects:

1) Age ≥ 18 years old;
2) Patient with clinically significant cataract with planned phacoemulsification cataract extraction and implantation of CT LUCIA 621P into the capsular bag;
3) Preoperative corneal astigmatism ≤ 1.00D;
4) Patient is willing and capable of providing informed consent;
5) Patient is willing and capable of complying with visits and procedures as defined by this protocol.

10.2.2. Exclusion criteria

Subjects meeting any of the following conditions in the case screening will be excluded from this study:

1) Preoperative CDVA > 4.7 or ≤ 0.3 logMAR ;
2) Corneal endothelial cell count less than 2000 cell/mm2;
3) Age under 18 years old;
4) Pregnant and lactating women;
5) Patients who attend other drug or medical device study;
6) Ocular disorder that could potentially cause a clinically significant future visual acuity loss;
7) Anterior segment pathology (e.g. chronic uveitis, iritis, aniridia, rubeosis iridis, anterior membrane dystrophies, poor pupil dilation, etc.)
8) Abnormal corneal finding (e.g. keratoconus, pellucid marginal degeneration, or irregular astigmatism, clinically significant corneal membrane dystrophies);
9) Any condition in the study eye that could affect IOL stability (e.g. pseudo-exfoliation, zonular dialysis, evident zonular weakness or dehiscence, etc.);
10) Any acute infection (acute ocular disease, external/internal infection, systemic infection);

11) History of any clinically significant retinal pathology or ocular diagnosis (e.g. diabetic retinopathy, ischemic diseases, macular degeneration, retinal detachment, optic neuropathy, amblyopia, strabismus, microphthalmia, aniridia, epiretinal membrane etc.) in the study eye that could alter or limit final postoperative visual prognosis;
12) Any previous intraocular and corneal surgery;
13) Uncontrolled glaucoma or IOP higher than 24mmHg under ocular hypertension treatment;
14) Current systemic or ocular pharmacotherapy that effects patients' vision;
15) Current pathology or condition that could be a risk for the patient according to the investigator opinion;
16) Patients unable to meet the limitations of the protocol or likely of non-cooperation during the study;
17) Patients whose freedom is impaired by administrative or legal order.

If both eyes are eligible, the dominant eye of the patient will be determined during the screening visit and will be selected as the study eye. Otherwise, the criteria of the investigator will be followed. The method to be used can be chosen by the investigator.

Commonly used methods are:

- Finger-point method

  With both eyes open, the patient points the finger at a small object in approx. 3m distance. The patient closes the right and the left eye one after another and will report with which eye open the object does not move. This is the dominant eye.

- Tube method

Paper tubes or any kind of other tools can be used for looking through the opening. The tube will be given to the patient who is asked to look through the tube. The patient will automatically use the dominant eye to look through the opening.

10.2.3. Subject withdraw criteria and procedure

If for any reason an investigator needs to discontinue/suspend a clinical investigation, the investigator should notify the site, and the investigator/site should immediately notify the sponsor and IRB/IEC and provide the sponsor and IRB/IEC with detailed reasons for the discontinuation/suspension of the study.

If a sponsor terminates or suspends a clinical investigation, the investigator should immediately notify the site and the investigator/site should immediately notify the IRB/IEC and provide the IRB/IEC with detailed reasons for the suspension/suspension.
If the IRB/IEC terminates or suspends the approval/favorable opinion of a study, the investigator should immediately notify the institution and the investigator/institution should immediately inform the sponsor and provide detailed written justification for the termination or suspension.

Drop-out criteria:

Withdrawal decided by the investigators, including the following circumstances:
1) if adverse events occur, so that continuation of the trial will impair the rights and interests of subjects, the investigators may decide to withdraw subjects from the trial;
2) if other complications or special physiological changes occur, the subjects should not continue the trial;
3) if subjects have poor compliance with the treatment, the investigators may decide to withdraw subjects from the trial;
4) if other circumstances occur, so that the investigators believe that the subjects should not continue the trial, the investigators may decide to withdraw subjects from the trial.

Withdrawal decided by the subjects, including the following circumstances:
1) the subjects are unwilling or impossible to continue the trial for any reason and tell the investigators they withdrawal from the trial;
2) although the subjects don't explicitly ask for withdrawal from the trial, they reject to undergo follow-ups, namely loss to follow-up.

The reason for discontinuation will be recorded. Subjects who are discontinued from the clinical investigation will still be a part of the analyses up until the point they are exited. When possible, all necessary clinical assessments will be performed prior to the subject exiting the clinical investigation even if the assessment was not scheduled at that particular visit.
There are no additional follow-up requirements once a patient has been withdrawn from the study.

Termination of the trial:

Termination of the trial refers to termination of the trial before completion of evaluation for

all the subjects according to the trial plan. If any of the following circumstances occurs, the trial may be terminated:

- A serious defect is found in the product during the trial;
- A major error is found in clinical trial protocol during the trial, so that the safety or efficacy of the product cannot be evaluated;
- A serious deviation occurs during implementation of the trial, so that the safety or efficacy of the product cannot be evaluated;
- ZEISS requires termination of trial due to any reason, such as financial, administrative and so on;
- National Medical Products Administration orders termination of the trial due to any reason;
- Ethics Committee requires termination of trial to protect the rights and interests of subjects.

After termination of the trial, new subjects will no longer be included, and the included subjects who have not departed from the hospital should be treated according to the agreement between ZEISS and investigators.

10.3. Evaluation Methods

10.3.1. Efficacy evaluation

[redacted]Primary evaluation indicator

- Evaluation indicator: Effectiveness rate of product 6 months after implantation.
- Evaluation method: Based on the situation of monocular CDVA ≥4.7 (≤0.3 logMAR) at 6 months postoperatively considered as effective, the effectiveness rate is not lower than target value (82.5%).

[redacted]

[redacted]

10.3.2. Safety evaluation

The safety evaluation indicators for this clinical investigation include:

(1) Corneal complications: Type, incidence and frequency (number of events) of postoperative corneal-related complications, such as corneal edema and corneal folds in test eyes.

(2) Corneal endothelial cell count: Postoperative corneal endothelial cell counts in test eyes;

(3) Anterior and posterior segment inflammations: Type, incidence and frequency (number of events) of postoperative anterior and posterior segment inflammations in test eyes measured at postoperative 1 day, 1 week ± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days;

(4) Fundus complications: Type, incidence and frequency (number of events) of postoperative fundus complications, such as macular edema and retinal detachment in test

eyes at postoperative 1 day, 1 week ± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days;

(5) Intraocular pressure: Postoperative intraocular pressure in test eyes at postoperative 1 day, 1 week ± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days;

(6) Posterior capsular opacification and Nd:YAG capsulotomy: Incidence and frequency (number of events) of postoperative posterior capsular opacification and Nd:YAG laser posterior capsulotomy in test eyes at postoperative 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days;

(7) Intraocular lens status: Type, incidence and frequency (number of events) of IOL decentration, tilt, rotation, dislocation, opacity, etc, in test eyes at postoperative 1 day, 1 week ± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days;

(8) Secondary Surgical Intervention

Incidence of postoperative secondary surgical intervention in test eyes;

(9) Adverse events and serious adverse events

Type, incidence and frequency (number of events) of adverse events (including but not limited to symptoms, signs and complications) and serious adverse events during the clinical trial;

(10) Device deficiency

Type, incidence and frequency (number of events) of device deficiency during the clinical trial;

10.3.3. Methods and timing to evaluate, record and analyze safety indicators

(1) Corneal complications: Corneal-related complications of test eyes at postoperative 1 day, 1 week ± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days are recorded according to the slit lamp microscope results. Any corneal edema found is graded according to the table below:

[redacted]

[redacted]

(2) Corneal endothelial cell count: Corneal endothelial cell counts in test eyes are measured with a corneal endothelial cell counter and recorded at postoperative 3 months ± 14 days and 6 months ± 30 days;

(3) Anterior and posterior segment inflammations: Anterior and posterior segment inflammations in test eyes are measured according to slit lamp microscope results at postoperative 1 day, 1 week ± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days. [redacted]

[redacted]

(4) Fundus complications: Fundus complications in test eyes are checked, recorded and reported at postoperative 1 day, 1 week ± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days (with slit lamp microscope), 1 month (OCT test);

(5) Intraocular pressure: Intraocular pressure in test eyes at postoperative 1 day, 1 week± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days are tested and recorded;

(6) Posterior capsular opacification and Nd:YAG laser posterior capsulotomy: The condition of posterior capsular opacification in test eyes recorded and reported according to slit lamp microscope results, and Nd:YAG laser posterior capsulotomy is recorded and reported at postoperative 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days . [redacted]

[redacted]

[redacted]

(7) Intraocular lens status: IOL decentration, tilt, rotation, dislocation, opacity, etc, in test eyes at postoperative 1 day, 1 week ± 1 day, 1 month ± 7 days, 3 months ± 14 days and 6 months ± 30 days are recorded according to slit lamp microscope results;

(8) Secondary surgical intervention: Cause, time, type and results of secondary surgical intervention in test eyes during the clinical trial are recorded;

(9) Device deficiency: Type and time of device deficiency during the clinical trial are recorded;

(10) Adverse events and serious adverse events: Adverse events and serious adverse events during the clinical trial are recorded.

[redacted]

[redacted]

10.4. Study device and control

This clinical investigation is a single-arm design with no control group. At the beginning of the study the investigation center is supplied with a standard set of CT LUCIA 621P. If the patient desires an CT LUCIA 621P also for the fellow eye (not the study eye) and it is according to the physician's opinion applicable also for the fellow eye, the IOL can be taken from this standard set as well without costs for the patient. However, only data on the study eye will be obtained by this study.

10.5. Equipment

Except for the equipment listed below, the tools for assessing the clinical investigation variables are to the discretion of the investigator and his standard of care. The technicians and investigators should be familiar with the instructions for use of the examination devices and have prior experience with the devices before using. The maintenance and/or calibration of the equipment shall be performed as applicable by the respective manufacturer's instructions for use.

For taking the biometry measurements the IOL Master 700 by Carl Zeiss Meditec AG shall be used. For VA measurement and determination of subjective refraction an ETDRS chart should be used whenever possible. [redacted]

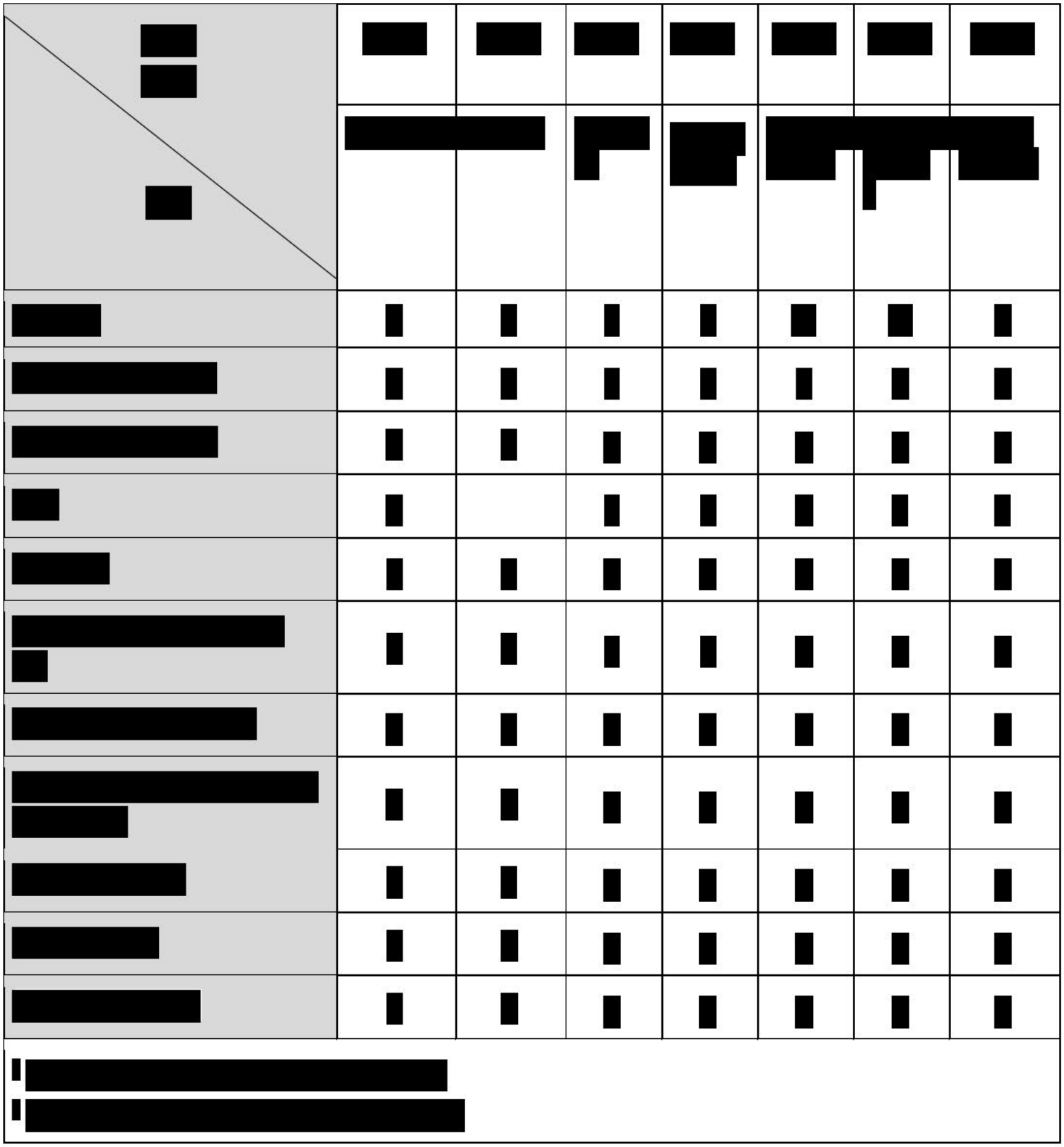
[redacted]

[redacted]

10.6. Study process

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]



10.6.2. Study execution

The study was conducted in accordance with the following procedures:

(1) Patient screening;
(2) Sign the informed consent form;
(3) Patient enrollment;

The investigators assign subject numbers sequentially according to the order in which the patients were seen.
(4) IOL implantation
(5) IOL implantation was followed up at 1d, 1w±1d, 1m±7d, 3m±14d, and 6m±30d.

10.6.3. V1 screening

Principal investigator and the authorized study-related staff on outpatient, interpretation of the test contents and the informed consent form, determine the participants' questions be answered completely, and have enough time to think about and willing to participate in after test, lead study-related staff and the participants are required to complete the signing of the informed consent, and indicate the date of informed consent in duplicate, lead study-related staff and participants each retain one copy.



The study-related staff will determine whether the subjects are suitable for inclusion in the study based on the collected data and examination results.

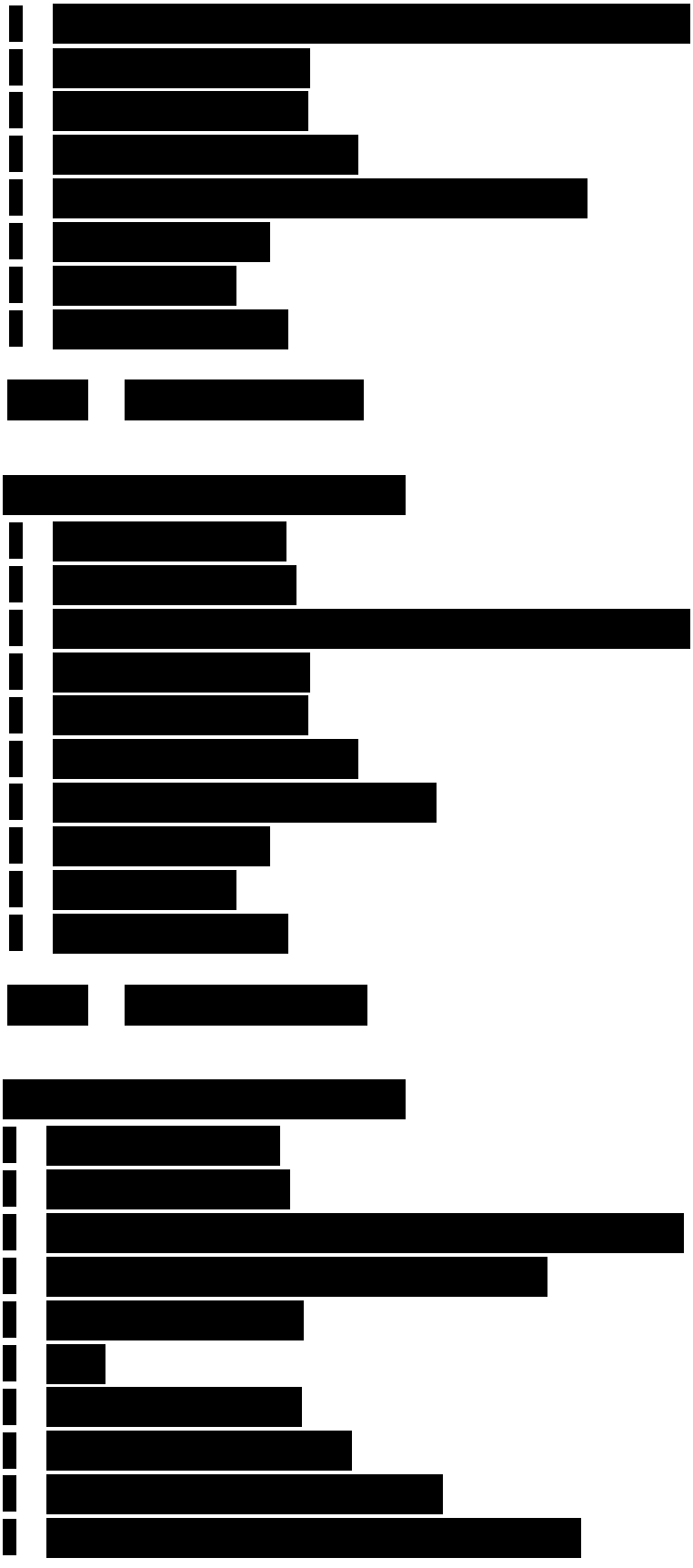
10.6.4. V2 Surgery

The cataract surgery and implantation of CT LUCIA 621P in the study eye will be performed by the investigator, according to his/her own surgery protocol and according to the manufacturer's instruction for use. No specific surgical procedure is involved.

[redacted]

If CT LUCIA 621P cannot be implanted during the procedure, the reason will be documented e.g. as device deficiency, adverse event or else and will be followed-up accordingly. In case of the device cannot be implanted or the patient does not meet any more the in- and exclusion criteria, the patient will be exited from the study.

[redacted]





[redacted]

10.6.10. Device use specification

Please refer to the “CT LUCIA 621P IOL instructions for use” for instructions on how to use the research group's products.

[redacted]

10.7. Bias control measures

All participating investigators will be trained in the use of the product and the operation of the protocol prior to the start of the real-world study to avoid bias among different investigators as much as possible.

In order to reduce the bias of clinical investigation results, uniform evaluation criteria were established for the evaluation of efficacy indicators, and investigators were arranged to evaluate the evaluation of efficacy indicators during the clinical investigation. All efforts will be made to keep the same study team during the duration of the clinical investigation. Select subjects with good compliance as much as possible during the clinical investigation to reduce the rate of subject drop-outs;

1) Investigators should explain in detail the preoperative, intraoperative and postoperative considerations of the test device to patients during the study;

2) The study model is single-centered, reducing bias due to geographical and hospital differences;

3) The study requires detailed collection of patient data for future statistical analysis to comprehensively judge the safety and efficacy of CT LUCIA 621P;

4) Data collection and management: an electronic data system will be used for data collection and management, a data management plan will be developed, logical verification procedures will be embedded to ensure the quality of the data, and data collection should include all confounding factors as much as possible to facilitate statistical analysis to correct for confounding factors.

11. Statistical considerations

11.1. Sample size calculation

This clinical investigation is designed as an open, single arm study.
Select Aier Eye Hospital of BoAo Hope City as the clinical research center for this study. After informed consent signed by the patients and satisfying inclusion criteria, the patients will be included in the clinical investigation.

The primary objective of this investigation is to show the effectiveness in regard to the monocular corrected visual acuity (CDVA) of CT LUCIA 621P 6 months after lens implantation. All subjects will be followed up preoperatively, intraoperatively, post-op 1d, post-op 1 week ± 1 day, post-op 1 month ± 7 days, post-op 3 months ± 14 days, and post-op 6 months ± 30 days.

[redacted] the non-inferiority margin should not be lower than 10%, and the expected target value of the product can be set at 82.5%.

Hypothesis that the overall effective rate of the product under study can reach 92.5% at post-op 6 months, under the condition of a bilateral significance level of 0.05 and a power of 80%, [redacted], using the Tests for One Proportion formula in PASS 15.



It is calculated that at least 94 patients are required, taking into account the 10% dropout rate, a total of at least 105 patients will be required for this study.

11.2. Analyzing datasets

(1) Full Analysis Set (FAS): It refers to a set of subjects determined on the basis of the Intention To Treat principle. It is the data set that includes all the subjects have used the test products. For the subjects for whom the primary efficacy endpoints are not observed, WCCF (Worst Case Carry Forward) strategy will be used to carry forward the missing data.

(2) Per Protocol Set (PPS): It refers to a subgroup of the subjects who complete the trial without serious protocol deviations (such as violation of inclusion criteria or exclusion criteria and loss to follow-up).

(3) Safety set (SS): It is defined with the same method as FAS. Therefore, SS is not separately defined in the analysis.

Analysis of primary efficacy endpoints will be performed based on the basis of FAS and PPS simultaneously; in addition, analysis of all the baseline demographic information and secondary efficacy endpoints will be performed on the basis of FAS; safety evaluation is also performed on the basis of FAS.

11.3. Subject exclusion criteria

11.3.1. Subject exclusion criteria/conditions

During sample size design, it is expected that the maximum possible drop-out rate during the trial will be 10%. The drop-out rate includes all the situations in which subjects cannot be included in the primary efficacy indicators analysis, which usually refer to the serious protocol deviations (with impacts on primary efficacy indicators evaluation) determined by investigators. The possible situations include: Subjects do not meet the inclusion criteria and meet the exclusion criteria; subjects do not use the test product; subjects use third-party products other than the test products; subjects do not complete primary efficacy indicators

visit the hospital according to the prescribed schedule; primary efficacy indicators follow-up time windows exceed the specified time limit; subjects receive the concomitant treatment that affects efficacy of test products and so on. The above situations will be included in the scope of total drop-out rate.

11.3.2. Processing Procedures

(1) The principal investigator or authorized study-related staff should contact the subject whenever possible, complete the assessment items that can be completed, complete the summary of study completion on the case report form, and notify the sponsor.
(2) Safety and efficacy data from uncommitted subjects must still be retained intact and analyzed according to the principles of appropriate statistical analysis (FAS and PP).

11.4. Statistical methods

The Statistical analysis is performed using SAS® 9.4 statistical software (or higher). Efficacy indicators will be analyzed for both the full analysis data set and the per-protocol data set, safety indicators were analyzed for the safety data set. All statistical tests will be performed using two-sided tests, and P values less than or equal to 0.05 will be considered statistically significant for the differences tested (except as noted).
This study is a one-arm design, mainly based on descriptive statistical analysis. The description of quantitative indicators will calculate the mean, standard deviation, median, minimum and maximum, lower quartile (Q1) and upper quartile (Q3), and classification indicators will describe the number of cases and percentages of various types.

[redacted]

11.4.1. Statistical analysis content

The actual number of subjects enrolled, drop-outs and excluded cases, demographic and other baseline characteristics, efficacy and safety analyses were analyzed.

11.4.2. Completion status and demography

Summarize the enrollment and completion of the center and make a list of drop-out cases. Different data set sizes, case distribution, comparison of total drop-out rate, and detailed list of incomplete causes. The patient's demographic characteristics (age, height, vital signs, etc.) and medical history will be described.

11.4.3. Evaluation indicator analysis

- Main evaluation criteria: effectiveness

Both PP analysis and FAS analysis will be used to evaluate effectiveness;
The 95% confidence interval (CI) of the difference between the two groups will be calculated for the treatment response rate six months after treatment. If the lower limit is greater than the target value of 82.5%, the study device will be considered to achieve the expected efficacy. Confidence interval estimation method adopts binomial distribution accurate method.

- Safety evaluation indicator:

The safety assessment will be analyzed on SS datasets.
The cases and times of surgical complications, adverse events and adverse reactions as well as the incidence of adverse events, serious adverse events, adverse reactions and serious adverse reactions will be described in a list.

[redacted]

- Secondary evaluation indicator:

PP analysis and FAS analysis will be performed for secondary evaluation indexes. The statistical analysis method follows the statistical method mentioned above.

11.5. Missing data and abnormal value handling

For the subjects who are not followed up or dropped out midway, when the efficacy results will be analyzed by the full analysis set (FAS), the missing values will be filled in by the Last Observation Carried Forward (LOCF) method. If there is no basis for filling, fill according to the worst filling method (i.e., treat as treatment failure).

12. Monitoring plan

ZEISS will commission the contract research organization (CRO) to monitor this trial, designate an appropriate number of qualified Clinical Research Associate, develop an appropriate monitoring plan, and perform monitoring before, during and after the trial to ensure that the rights and interests of subjects in the trial are protected, the data in the trial records and reports are accurate, true and complete, and the trial is conducted in accordance with the approved protocol, GCP and other relevant laws and regulations. [redacted]

13. Data management

Data Management procedures will follow applicable regulations, [redacted]

13.1. Data Reporting

Verified and validated electronic data capture (EDC) will be utilized for capturing objective data. Subjective data will be captured on paper and entered into the eCRF by designated study site staff during this clinical investigation. The eCRF application will be accessible by connecting to a dedicated server via a secure website. Each member of the study team has a password protected login with an individual username identifying the single user. Depending on the assigned tasks in the clinical investigation only the access rights necessary to complete the assigned tasks are given by allocating each user to one out of a set of pre-defined user roles. [redacted]

Worksheets will be provided by the sponsor, if necessary, for each eye enrolled in the clinical investigation. In order to facilitate data entry, the worksheets coincide with the data entry pages (eCRFs) in the EDC system. When the site decides to use the worksheets, those will serve as the source data. The appropriate worksheets will be completed and initialed or signed where indicated at each examination. All worksheets will be completed in a legible manner in black/blue ink. Alternatively, the native subject records will serve as source data.

Any corrections to the worksheets or other source data will be made by drawing a single line through the incorrect entry, recording the correct information, and initialing and dating the

change. The study worksheets or the native subject record as well as the data entered in the EDC system will be reviewed by the Study Monitor.
Data entry into the eCRF is done in a pseudonymized manner. Each subject will be identified by a subject code not revealing the actual patient. Data entry into the eCRF is change-controlled via an extensive electronic audit trail within the EDC system. Automated checks for completeness and consistency are performed directly on-line during data entry. In addition, manual quality control will be performed by the data manager. Both these check steps lead to system queries, that need to be answered within the EDC system used by the investigator or designee. [redacted] All worksheets and data entered into the EDC system will be reviewed for completeness and evident recording errors will be rectified by contact with the appropriate clinical site. Computerized data checks will be used to identify unusual data entries for verification prior to statistical analysis. Queries resulting from automatic or manual consistency checks need to be answered by the investigator or designee directly within the EDC system.

13.2. Completion of case report form

[redacted] The entire clinical trial process should be carried out with strict operations. The investigators shall truthfully, carefully and seriously record various contents in eCRF according to the instructions for completion of case report form to ensure that the contents of the case report form are complete, authentic and reliable. All the clinical trial data that shall be recorded according to the protocol should be verified to ensure the reliability of the data and to ensure that the conclusions of the clinical trial are derived from the source data. Appropriate data management measures shall be taken during various stages of clinical trial and data processing.

13.3. Data review

Review after completion of data entry and inspection, and complete the final definition and judgment of the analysis community.

13.4. Database Locking

When the following conditions are met, the database can be locked.

- All the data have been entered into the database.
- All queries have been resolved.
- The analysis group has been defined and judged.

14. Risk and benefit analysis

14.1. Device use risk

A complete list of warnings, undesirable side effects and residual risks is included in the IFU. The risks associated with the use of the CT LUCIA 621P are comparable with the use of any other currently available monofocal IOL.

Cataract surgery complications are few and cataract surgery is among the most common and most successful surgical procedures performed today. The conclusion of overall risk assessment is that CT LUCIA 621P does not exhibit undesirable or intolerable risks.

14.2. Benefits to patients

Cataracts cannot be treated without surgery. The only way to treat cataracts is a surgery to remove the clouded lens and replace it by an artificial lens implant (intraocular lens) which restores vision. Meanwhile, modern intraocular lenses have been used as permanent implants for many years. Complications are rare and exchange of the implant is usually not required. Except for aphakia correction, conservative methods to correct myopia and hyperopia include eyeglasses and contact lenses. Other options like refractive laser treatments are also surgical. Laser refractive surgeries like PRK (photorefractive keratectomy), LASEK (laser-epithelial keratomileusis) and LASIK (laser in situ keratomileusis) are able to correct most visual refractive defects in certain diopter ranges. These procedures change the shape of the cornea by corneal ablation which leads to the desired correction of ametropia.

Pseudophakic eyes are unable to accommodate and reading glasses or glasses for intermediate distances will be required in addition to an implanted monofocal IOL. Bifocal or trifocal IOLs allow near and/or intermediate vision in addition to the far vision.

The benefit of subjects implanted with the CT LUCIA 621P IOL is the restoration of far visual acuity.

New lens designs and materials for artificial intraocular lenses which are intended to be implanted into the capsular bag after cataract extraction and improvement of surgery technique have greatly reduced the risks of complications during and after cataract surgery. Preloaded IOLs increase the safety of IOL implantation by reducing possible contact with external contaminants.

Most adverse events result from the cataract surgery rather than from the devices. While many identified side effects are permanent, the vast majority are minor and can be corrected by wearing glasses, or in the worst case, by additional surgery.

The device's literature, essentially the IFU, describe the intended use that is supported by sufficient clinical evidence. In addition, the IFU contains all the important information to reduce the risk of use error, information on residual risks and their management.

The only disadvantage arising from participation in the clinical trial is that the subjects must spend an additional visit at the clinic. As the subjects are informed on this and give their informed consent this seems to be acceptable. The main benefit is that the subject will benefit from a comprehensive examination of your eye. All in all, the advantages in the planned clinical trial outweigh the disadvantages.

The benefits and risks associated with cataract extraction and IOL implantation are well understood by ophthalmic surgeons. The safety and effectiveness profile of monofocal IOLs, such as the CT LUCIA 621P, has been well established. Data collected from the previous clinical trials with an IOL identical to CT LUCIA 621P and an equivalent delivery system, indicated a similar risk profile as currently-marketed foldable hydrophobic IOLs. Thus, the benefits of the CT LUCIA 621P outweigh the risks for the proposed indications for use (i.e. visual correction of aphakia in adult subjects in whom a cataractous lens has been removed).

15. Device Accountability

The clinical site will be provided with the investigational device, which can be identified by a unique serial number. The investigational device will be individually packaged. The labelling is according to MDR [redacted] and all other applicable local regulations.

Each IOL package will contain the following items:

- IOL CT LUCIA 621P
- Patient Implant Card
- Labels containing the IOL information and unique serial number

The device will be available in the diopter range of 0.0 D to 34.0 D in 0.5 D increments for this study.

Site staff shall confirm receipt by following the study-specific procedures and retain all required documents in the study records. Throughout the study, the site must also maintain records of investigational products used for each subject. This record must be made available to the study monitor for the purpose of verifying the accounting of investigational products supplies. Any discrepancies between the observed disposition and the written account must be recorded and explained. All investigational products must be accounted for by the sponsor or representatives and must not be used in an unauthorized manner.

The investigator is responsible for the proper disposition of all unused investigational products at the end of the clinical investigation, according to the instructions provided by the sponsor.

16. Clinical investigation quality control

The sponsor and the principal investigator shall ensure the quality of the study. [redacted]

[redacted]

16.1. Monitoring and auditing

The Clinical Research Associate appointed by ZEISS conducts regular on-site monitoring of the site to ensure that the trial is implemented in strict accordance with all aspects of the protocol. In addition, the Clinical Research Associate inspect the source data to ensure consistency with the eCRF.

[redacted]

16.2. Data Management and Retention

Source data of the trial include the signed informed consent forms, test device distribution records, laboratory test reports, case records and other relevant records. [redacted]

[redacted]

[redacted]

17. Clinical investigation EC and informed consent

17.1. Ethical considerations

The study is conducted in accordance with the Helsinki Declaration of Ethics, the International Standard ISO 14155[redacted], the Code of Practice for the Quality Management of Clinical Trials of Medical Devices, and the regulations related to clinical studies. According to the regulations of clinical studies and the ethics committee, the final version of the clinical investigation protocol and other related documents will be reviewed and approved by the ethics committee before the start of the study, and the study will be conducted in accordance with the following:

1.The sponsor, principal investigator and study-related personnel shall not coerce or unduly influence subjects and other study-related personnel.

2.The sponsor's subsidy for the subject's participation in the clinical investigation must not unduly influence the subject's participation.

3. The sponsor shall assume responsibility for all medical injuries arising from the execution of this clinical investigation program and shall be liable for all damages in the event of a study-related health injury and shall make appropriate and specific medical care arrangements for subjects, as detailed in the clinical investigation report. This does not apply to the following situations.

(1) Events caused by meaningful deviations in the protocol;

(2) Events caused by intentional or gross negligence of the subject, the principal investigator, or the institution.

4. The principal investigator and all investigators involved in the study must be suitably qualified and must be aware of and willing to comply with the Declaration of Helsinki.

5. The principal investigator or authorized investigator shall explain to volunteers who may participate in this clinical investigation the contents of the informed consent form, including the purpose, methods, procedure, expected effects, possible risks and any possible discomfort of this study, and give the volunteers sufficient time to think about whether they wish to participate in this study.

6. Subjects must participate in this study of their own free will, without undue inducement or coercion.

7. Subjects who are willing to participate in this study are asked to sign and date an informed consent form together with the principal investigator after they have fully understood the contents of this study.
8. If there is a need to revise the study protocol and the revision will affect the study process or the subject's rights and interests, etc., the informed consent form must be updated and the subject's consent reobtained before the subject is allowed to re-sign the informed consent form.

17.2. The informed consent process

The dedicated ICF for this trial should be subject to review and approval by the ethics committee. ZEISS provides an ICF sample to each site. The ICF sample may be modified by the sites to meet specific requirements; however, the ICF must include all the elements that should be included according to applicable regulations. [redacted]

18. Adverse event and device deficiency reporting

18.1. Definition of adverse events and reporting requirements

An adverse event (AE) is any untoward medical occurrence in a clinical trial and which does not necessarily have a causal relationship with the test medical device.

[redacted]

[redacted]

18.2. Definition of serious adverse events

Serious adverse events refer to the events leading to death or serious deterioration of health conditions of subjects during clinical trials, including fatal illness or injury, permanent damage to physical structure or function, hospitalization or prolonged hospitalization, medical treatment or surgical intervention to avoid permanent damage to physical structure or function, fetal distress, fetal death or congenital abnormalities, congenital defects and other events.

Death should not be reported as an adverse event, but should be reflected as the outcome of a particular serious adverse event.

18.3. Report procedures and contact information

All the adverse events occurring during the trial must be truthfully recorded in the adverse event table and eCRF after detection of these events. Investigators should provide targeted treatment of adverse events and perform follow-ups until the symptoms disappear or become stable. [redacted]

[redacted]

18.4. Device deficiency

Device deficiency refers to the unreasonable risks that may endanger human health and life safety under normal use of a medical device during a clinical trial, such as wrong labeling, quality problems and malfunctions.

[redacted]

19. Clinical investigation protocol deviation and revision

19.1. Deviations from the study protocol

19.1.1. Definition

Failure to perform clinical investigation in accordance with a protocol approved by the Ethics Committee, or failure to perform clinical investigation in a process that does not comply with clinical investigation regulations; Its contents include, but are not limited to, the following situations:

1. Subjects who entered the study were not eligible for the study.
2. Subjects who received the wrong treatment or assessment.
3. Failure to execute the study in accordance with the clinical investigation protocol.

19.1.2. Handling procedure

The sponsor shall notify the principal investigator and the relevant study-related staff to perform the clinical investigation in accordance with the study protocol approved by the Ethics Committee, and if it is not carried out in accordance with the study protocol, the following matters shall be completed:

[redacted]

All test deviations must be notified to the sponsor, who is responsible for analyzing and assessing the importance of the deviation, which can be classified according to the following different levels:

[redacted]

Serious deviations and persistent deviations must be reported to the Ethics Committee.

In case of emergency, the safety of the subjects must be the priority. If the clinical investigation protocol is violated as a result, the incident must be recorded in detail in the study deviation table and the sponsor and the ethics committee must be informed as soon as possible.

19.2. Amendment of the study protocol

This trial shall not be initiated until it is reviewed and approved by the ethics committee of the sites. Any modification to clinical trial protocol during the trial shall not be implemented until it is approved in writing by the ethics committee.

Clinical trial protocol shall be strictly executed after it is approved by the ethics committee. If it is really necessary to supplement or revise the protocol after initiation of the trial, investigators and ZEISS should reach an agreement through negotiations, submit the proposal of amendment to ethics committee, and perform the revision after it is approved by the ethics committee. The revision of the protocol shall be carefully recorded, and the contents of the record shall include the specific contents and reasons of revision, the correspondence for application for re-approval of ethics committee, the approval document from ethics committee and so on.

Deviations from clinical trial protocol should be regularly inspected to determine whether it is necessary to amend or cancel the protocol.

[redacted]

[redacted]

22. Confidentiality

1. The principal investigator and all study-related staff shall adhere to the principle of confidentiality of subject information and shall not disclose any information about the subjects to third parties.
2. Only the principal investigator and authorized study-related staff will have access to the original medical records of the subjects for the purpose of confirming the study procedures and related data.
3. In this study, subjects will be given a screening number to represent their identity upon entry into the study and a random number to represent their identity if they are identified in the study.
4. In the event of publication of the results of the study, the identity of the subjects will remain confidential, and the investigators involved will undertake not to breach the confidentiality of the subjects' identities.
5. To ensure that the process and data of this study comply with relevant laws and regulations, the central authority, the quality management personnel (monitors, auditors) assigned by the original manufacturer, the hospital and its ethics committee may review the source data or documents during or after the study, but all relevant personnel will adhere to the principle of confidentiality of subject information.

23. Responsibilities of each party

23.1. Statement of Compliance

This clinical trial is conducted in compliance with the World Medical Association Declaration of Helsinki and relevant national laws and regulations. The sites have passed the ethical review according to the requirements of GCP, and the rights, interests, safety, health and privacy of clinical trial subjects are protected in accordance with the ethical principles specified in GCP.

The proposed clinical investigation is subject to all local and national applicable governmental rules and regulations concerning the conduct of clinical investigations on human subjects. It will be performed as an interventional clinical investigation as per local regulations.

All parties involved in the conduct of the clinical investigation share the responsibility for its ethical conduct in accordance with their respective roles in the clinical investigation.

This includes, but is not necessarily limited to, the approval by the EC/IRB and CA; obtaining informed consent; monitoring the conduct of the clinical investigation, the completeness of the worksheets, and accuracy of data entered into the EDC system in eCRFs, as may be employed, by the sponsor or its designee(s); and record retention by the sponsor.



[redacted]

[redacted]

23.5. Insurance

For this clinical investigation a specific insurance, covering the subjects for clinical-investigation-related risks which arise from participation in this clinical investigation will be contracted. An insurance for commuting accidents will be arranged, if applicable. The insurance will be taken out by the sponsor. All subjects will get the specific information before they sign the patient informed consent.

23.6. Clinical Investigation Financing

The sponsor will assume the cost related to the examinations, visits, which are different from standard of care treatment. The caring costs are detailed in the financial contract related to this clinical investigation.

24. Vulnerable Population

No vulnerable population will be included in this investigation.

Pregnant subjects are excluded from this study. If pregnancy occurs during the trial, this is not reportable as an adverse event. However, complications may be reportable and will be decided on a case-by-case basis.

[redacted]

26. Other Content

Not applicable.

[redacted]

[redacted]

