RESEARCH SUMMARY

Reserved for the promoter		ID RCB No	CPP No	CNIL or MR No	
		2022-A00702-41	22.01643.000097	MR003 Ref 2219976 v 0	
	Regulatory qualification	☐ RIPH of the 1st drug ☐ RIPH of the 1st innovative therapy drug ☐ RIPH of a medical device ☐ RIPH of 1° excluding health products		☐ 2° RIPH with minimal risks and constraints ☒3° RIPH nointerventional	

Summary of the research protocol for RIPH 3 comprising only qestionnaires and interviews decree of December 21, 2018

FULL TITLE: Study of lidocaine gel anesthesia for intravitreal injections

Short title: ANGLIA

VERSION N°5 03/06/2022

☒**Monocentric** ☐**National**

☐ **Multicentric** ☐**European/International**

Promoter:	**Contact: Anne BARRUCAND**
SELARL Ophtalliance Network of 46 ophthalmic physicians and surgeons practicing in 11 centers in the west of France Address: 88 Rue de Hauts Pavés 44000 Nantes	Methodologist- biostatistician Institut ophtalmologique de l'Ouest (IOO) Jules Verne Clinical Research Department **PI: Dr. Jean-François LE ROUIC** **Email: anne.barrucand@ophtalliance.fr** **Phone: +33 6 72 08 34 15**

Compliance of this request for an opinion with the procedure provided for in II of Article R.1123-20 of the Public Health Code:

– This research only includes data collected by questionnaire(s) or interview(s):

Yes ☒

No ☐

– This research has no consequences for the participants either in terms of safety or modification of the usual care:

Yes ☒

No ☐

– This research is risk-free and the disadvantages for the people participating in the research are negligible:

Yes ☒

No ☐

– The collection and processing of data implemented in this research complies with the reference methodology MR003 approved by the CNIL:

Yes ☒

No ☐

HISTORY OF PROTOCOL UPDATES

VERSION	DATE	REASON FOR UPDATE
4	**06/03/2022**	**ASKED OF MODIFICATION OR OF INFORMATION FROM THE CPP**

TABLESUBJECTS

OphtAlliance

I – ADMINISTRATIVE INFORMATION

RESEARCH

RESEARCH TITLE	**Study of lidocaine gel anesthesia for intravitreal injections**
SHORT TITLE OF RESEARCH	**ANGLIA**
REGISTRATION NUMBER (ID-RCB)	**2022-A00702-41**

PROMOTER

NAME–OR–LEGAL FORM AND NAME	Ophtalliance SELARL
COMPLETE ADDRESS	88 Rue de Hauts Pavés - 44000 Nantes
PHONE	+33 2 51 77 75 27

PRINCIPAL INVESTIGATOR

NAME, FIRST NAME	**Dr LE ROUIC Jean-François**
FUNCTION	***Qualification: ophthalmologist*** ***Specialties*:** - Vitreoretinal surgery - AMD (Age-Related Macular Degeneration) - Medical pathologies of the retina - Cataract surgery - IVT (Intravitreal injections)

RESEARCH LOCATION	Institut Ophtalmologique de l'Ouest (IOO) Jules Verne 2-4 Route de Paris – 44300 Nantes
PHONE	+33 2 28 44 33 73
EMAIL	jflerouic@gmail.com

II – CONTEXT AND JUSTIFICATION OF THE RESEARCH: RATIONALE PRESENTING THE CONTEXT AND THE RESEARCH HYPOTHESES

Intravitreal injections (IVT) of anti-vascular endothelial growth factor (VEGF) and corticosteroids are the standard treatment to combat various retinal pathologies such as neo-vascular age-related macular degeneration (AMD), macular edema occurring during retinal vein occlusions, diabetic macular edema, high myopic neovascularization,…[1]

An injection of these anti-factors stops the proliferation of abnormal vessels and reduces macular edema [2].

These injections are very effective but must be renewed regularly (on average every 2 months), for several years. Despite the anesthesia (usually topical) administered before each injection, some patients complain of feeling discomfort or even pain when placing the blepharostat (the device that keeps the eyelids apart) and inserting the needle through the sclera.[3]

Although the percentage of patients perceiving severe pain during an IVT session is low [4], pain management for these patients represents an important issue not only for their comfort but also for treatment compliance. It is important to reduce it effectively to improve patient management. The patient requires pain management when the score is greater than 3-4/10 on the VAS (Visual Analogue Scale which is the reference scale)[5].

Topical anesthesia using anesthetic drops (Tetracaine® or Oxybuprocaine®) is the reference method.

It is also possible to offer patients topical anesthesia by the instillation of eye drops (Tetracaïne® or Oxybuprocaïne®) associated with so-called "improved" topical anesthesia » by the preoperative instillation of a drop of lidocaine gel: Ophtesic®. This protocol has obtained the favorable opinion of the ANSM but is currently little used. [6]. Several studies have proven the safety and efficacy of lidocaine gel for anesthesia during eye surgery [6–9]

In our practice at the IOO, we use the reference method as first intention, and we offer lidocaine gel to people complaining of having had pain during previous IVT sessions.

This practice carried out at the IOO has never been evaluated. In addition, there are several studies dealing with pain at the time of injection [10–17] and comparing different anesthetics [18–20], however they were carried out on a non-targeted population.

According to the HAS report[21]: “OPHTESIC 20 mg/g (lidocaine), ophthalmic gel in a single-dose container, does not provide any improvement in actual benefit (ASMR V) compared with anesthetic eye drops in the topical anesthesia during ophthalmic procedures. ". However, in our practice, patients who received topical anesthesia for IVT using anesthetic drops (Tetracaine® or Oxybuprocaine®), associated with a drop of lidocaine gel, report less pain, especially when placing the blepharostat.

The aim of this study, which includes two parts, is to better understand the prevalence of pain and its intensity during IVT and then to evaluate the effectiveness of the protocol using a drop of lidocaine gel on a targeted population (patients with a VAS score ≥ 4/10) in order to improve the management of patients complaining of severe pain during the injection.

We will first assess the perception of pain and its intensity during IVT using questionnaire 1. Once this step has been completed, we will suggest that the patients who have felt the most pain (VAS ≥ 4/10) and who have chosen to switch to anesthesia with lidocaine gel will again assess the pain felt with questionnaire 2.

The study will therefore consist of analyzing the responses to a survey carried out using 2 questionnaires offered during 2 IVT sessions for the same patient:

- **Quiz 1**: survey carried out in the context of anesthesia with the reference method
- **Quiz 2**: survey carried out during improved anesthesia (protocol to be evaluated): Tetracaine® or Oxybuprocaine® eye drops combined with a drop of lidocaine gel.

Pain being strongly correlated with the psychological state of the patient, and his degree of anxiety before the injection [13] , a psychological evaluation of the patient before the intervention will be carried out using the HAD Anxiety Scale (Hospital Anxiety and Depression Scale) by AS Zigmond and RP Snaith (French Translation JL Lépine) during the 2 questionnaires.

III – OBJECTIVES AND JUDGMENT CRITERIA

MAIN OBJECTIVE	The main objective of this study is to evaluate the relief provided by so-called "improved" topical anesthesia by the preoperative instillation of a drop of lidocaine gel in addition to a drop of the anesthetic Tetracaine® or Oxybuprocaine® in patients perceiving severe pain during IVT compared to the reference anesthesia protocol.
MAIN JUDGMENT CRITERIA	EVA Score: The figure will be rounded to the nearest millimeter Comparison of the pain score felt during the injection during the 1st evaluation (with conventional anesthesia) with the pain score obtained during improved anesthesia.
SECONDARY OBJECTIVES	1- Confirmation of pain relief with the score obtained on the simple verbal scale 2- Description of the prevalence and intensity of pain experienced by patients during IVT 3- Description of the psychological state of the patient during a IVT and validation of score stability

	4- Evaluation of the security of the protocol
SECONDARY JUDGMENT CRITERIA	1. Descriptive statistics of the verbal scale score 2. Descriptive statistics of pain scores recorded during pain assessment using VAS for IVT with conventional topical anesthesia 3. Descriptive statistics of the psychological state of the study population. Comparison of the scores obtained between the 2 assessments 4. Description of possible side effects

IV. - ORGANIZATION OF THE STUDY:

A. - SYNTHETIC DESCRIPTION OF THE STUDY SCHEME

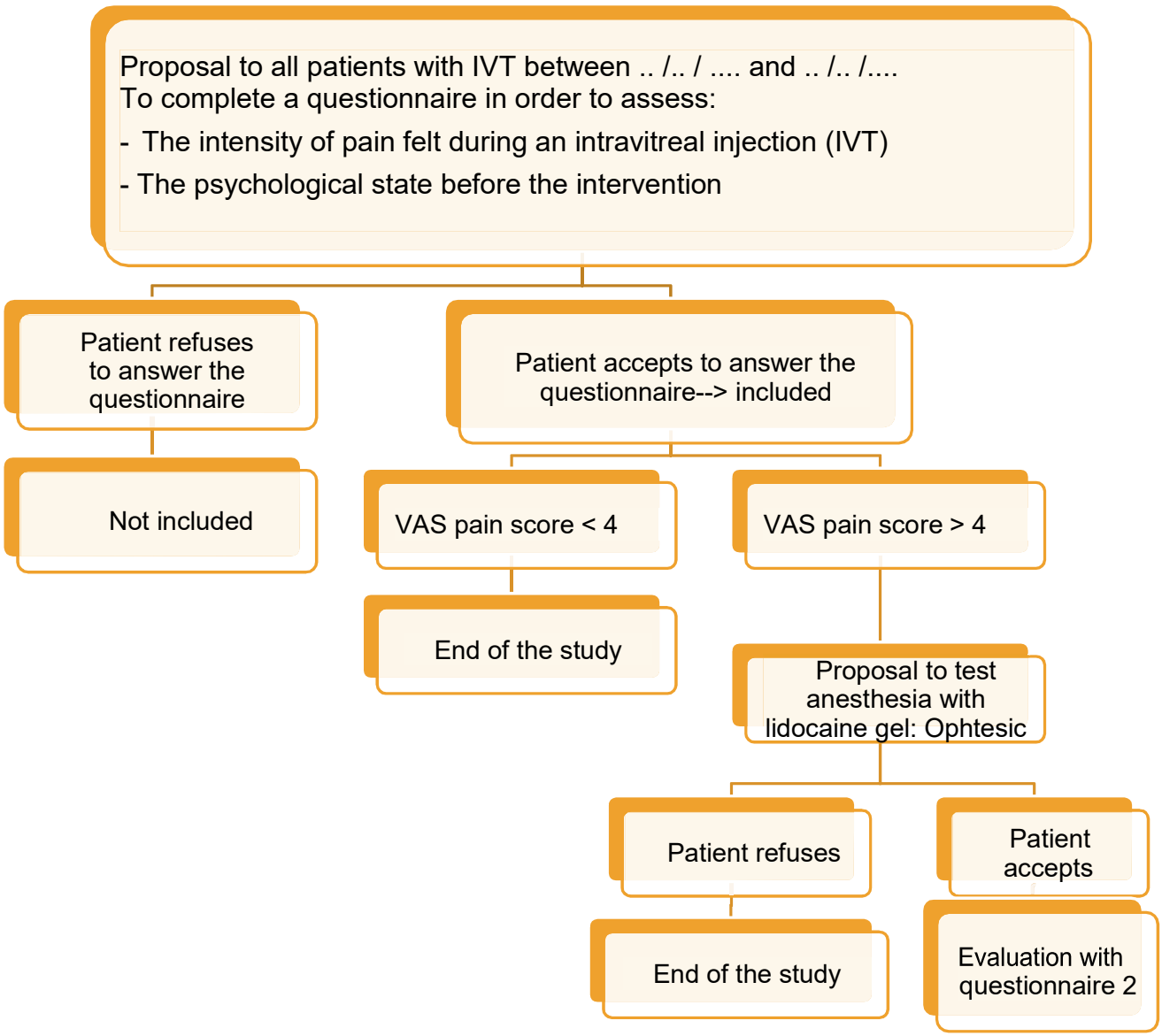
SYNTHETIC DESCRIPTION	Monocentric study **1. Initial evaluation of the pain felt by patients during an intravitreal injection (IVT) as well as their psychological state before the intervention** The basis for this evaluation is a questionnaire completed by the participants before and after the injection. It is composed : - A psychological assessment (the HAD Anxiety Scale (Hospital Anxiety and Depression Scale - Authors: AS Zigmond and RP Snaith - French translation JL Lépine) completed by the patient before the IVT - 2 measures for pain assessment using VAS: o One to assess the pain felt when placing the blepharostat o The other to assess the pain felt when inserting the needle: answer given just after the IVT session.

	2. Selection of patients who felt the most pain (EVA ≥ 4/10) and proposal to pass with the protocol: a drop of Tetracaine® or Oxybuprocaine® and a drop of lidocaine gel. **Evaluation of pain and relief of patients during IVT with so-called "enhanced" topical anesthesia.** The basis for this evaluation also consists of a questionnaire completed by the participants before and after the injection. It is composed : - A psychological assessment (HAD Anxiety Scale (Hospital Anxiety and Depression Scale - Authors: AS Zigmond and RP Snaith) completed by the patient before IVT - Of 2 measures for the evaluation of pain using VAS: one to evaluate the pain felt when inserting the blepharostat and the other to evaluate the pain felt when inserting the needle: response performed immediately after the IVT session. - An assessment of pain relief: Simple verbal scale (1 for placing the blepharostat and the other for inserting the needle) The answers to the questionnaires will be collected by one of the nurses (TEC or ARC) and the ARC orthoptists and the anonymized data will be sent to the biostatistician of the clinical research department for analysis.
DESCRIPTION OF THE PROCEDURE OF THE IVT	The injection is performed in the operating room dedicated to IVT at the Jules Verne clinic <u>Anesthesia procedure: reference method:</u> -Instillation of a drop of topical anesthetic: Tetracaine® or Oxybuprocaine®

	- Initial cleansing of the surface of the patient's periocular skin with povidone iodine scrub. Rinse with saline solution and dry with sterile compresses. - Instillation on the conjunctiva of a drop of povidone iodine in a 5% ophthalmic solution. After 2 minutes. - Instillation of 2 drops of anesthetic: Tetracaine® or Oxybuprocaine® <u>Anesthesia procedure: with lidocaine gel:</u> - Instillation of a drop of topical anesthetic: Tetracaine® or Oxybuprocaine® - Initial cleansing of the surface of the patient's periocular skin with povidone iodine scrub. Rinse with saline solution and dry with sterile compresses. - Instillation on the conjunctiva of a drop of povidone iodine in a 5% ophthalmic solution. - Instillation of lidocaine gel drop <u>Procedure common to both anesthesia protocols</u> - Preparation of the syringe containing the product to be injected in a sterile manner by the operator as close as possible to the injection - Placement of a sterile drape isolating the patient's eye - Placement of a blepharostat so as to limit the risk of contact between the needle and the free edge of the eyelids or eyelashes. - IVT between 3.5 and 4 mm from the limbus: slow injection of the product - Slow needle withdrawal.

COURSE OF THE STUDY	The research includes 2 parts: - **Evaluation of the prevalence of pain and its intensity during an IVT.** Cohort: For 15 days: distribution of the information letter during the consultation to all patients requiring IVT - **Evaluation of the effectiveness of the protocol using a drop of lidocaine gel** Cohort: patients experiencing pain requiring management (VAS score ≥ 4) and who wish to switch to the enhanced anesthesia protocol

	Recruitment of patients will be done on the voluntary participation of patients. The information letter will be submitted for consultation and the evaluation will be scheduled during the next IVT session so that the person has time to reflect before making their decision. Participants may withdraw their consent at any time.



B- METHODOLOGY OF QUESTIONNAIRES / INTERVIEWS

AWARDING PROCEDURE	**Questionnaires administered by:** ☐ Mail ☐ Internet ☐ Phone ☒ Face to face: during the IVT ☐ Other (explain, list) : …… **Questionnaire administered in:** ☐ Once ☒ Several times (specify the number of awards): 2 **Questionnaire type:** ☒ Validated ☐ Invalid – if validated, indicate the origin of the validation: For assessment of psychological state and anxiety before the intervention: HAD Anxiety Scale (Hospital Anxiety and Depression Scale - Authors: AS Zigmond and RP Snaith - French translation JL Lépine) For pain assessment: Analogue Visual Scale (EVA): ranging from 1 to 10 cm For assessment of pain relief: Simple verbal scale. – if not validated, justify: **Does the research also involve collecting retrospective data:**

	☒ yes ☐ No – if yes, justify: The number of previous IVTs, the pathology requiring the IVT, eye treatments, allergies, history of eye surgery, use of oral analgesics will be collected by the nurses from the patients' medical files.
INTERVIEW	**Methods of realization :** ☒ Individual interview ☐ Collective interview **Interview carried out in:** ☒ Frontface to face during the IVT session ☐ video conference ☐ phone ☐ Other (explain, list) : **Interview carried out**: ☐ once ☒ several times Number of awards: 2 **Type of maintenance:** ☐ directive ☒ semi-directive ☒non directive **Registration**: ☒No ☐ yes

STATISTICAL DATA ANALYSIS	Pseudo-anonymized data will be collected on an Epi-data spreadsheet The analysis will be carried out using the statistical analysis software: R version 3.4.4 (R-project) **Descriptive statistical analysis** The results will be presented: - As mean +- sd (min; max) for quantitative variables - As a percentage for qualitative variables **Main criterion:** Comparison of the score obtained during the 1st evaluation (with conventional anesthesia) with the score obtained during improved anesthesia: paired T-test **Other analyses:** **Data that were found statistically correlated to the result:** - **The psychological state of the patient**[13.22] Comparison of the scores obtained between the 2 evaluations of the psychological state (HAD scale): paired t-test - **The injection site** [23] - **The number of prior IVTs**[23] - **gender and age**[24] Comparison of pain scores according to potentially correlated factors: multivariate analysis
REFERENCES OF THE RESPONSIBLE BIOSTATISTICIAN	**Last name First Name :** BARRUCAND Anne Address: Jules Verne West Ophthalmological Institute Clinical Research Department 2-4 route de Paris - 44300 NANTES

	Telephone: 06 72 08 34 15 Email:anne.barrucand@ophtalliance.fr

V. - INFORMATION RELATING TO THE IMPLEMENTATION OF THE RESEARCH:

PLACES OF RESEARCH	Ophtalliance Ophthalmology Center: - Ophthalmological Institute of the West Jules Verne Clinic 2/4 Route de Paris – 44300 NANTES
PROVISIONAL RESEARCH TIMETABLE	Start of study: Upon receipt of the opinion of the CPP Duration of the inclusion period: 15 days (for phase 1 and for phase 2: these are the patients selected from the phase 1 cohort) End of study report: August 2022
NUMBER OF INTERVIEWEES	1st part: All patients who are called for an IVT over a period of 15 days and who have given their consent to participate in clinical research: approximately 300 patients 2nd part: patients who felt severe pain during IVT (VAS ≥ 4/10) and who consent to test another protocol (estimate: 40 to 60 patients)
INCLUSION CRITERIA 1st QUESTIONNAIRE	- Over 18 - Participants having all their capacities of discernment and being able to answer the questionnaires - Patient summoned for an intravitreal injection of an anti-VEGF drug in liquid form (ranibizumab, aflibercept, bevacizumab) - Indication for injection: painless retinal pathology (age-related macular degeneration, retinopathy diabetic, macular edema on venous occlusion

	retinal, neovascular membrane on high myopia, or other). -Note information given to the patient and collection of signed non-objection
EXCLUSION CRITERIA 1st QUESTIONNAIRE	- Persons cited in articles L.1121-6 to L.1121-8 of the CSP - Patients not followed at the IOO Jules Verne or at the Hauts Pavés practice. - Eye pain before the procedure - Intravitreal injections performed with oftriamcinolone acetonide - Intravitreal injections performed with a larger gauge needle (Ozurdex® or Iluvien ®) - Intravitreal injections performed using a disinfectant other than povidone iodine - Patients for whom the protocol with lidocaine gel in anesthesia is already used - Any cortisone injection - Any uveitic inflammatory pathology whether immunological or infectious - Anyone under systemic treatment with cortisone or morphine and its derivatives
INCLUSION CRITERIA 2nd QUESTIONNAIRE	- Patient with a VAS score during the 1st assessment: VAS ≥ 4/10 - Patients who have given their consent to switch to the protocol with the addition of lidocaine gel (information letter provided and collection of non-objection)
EXCLUSION CRITERIA 2nd QUESTIONNAIRE	- Eye pain before the procedure - patient takingadditional or different analgesic treatment compared to the evaluation of the 1st questionnaire - Known allergy to lidocaine or any of the other ingredients of Ophtesic (hypromellose (E464) type 2910, sodium hydroxide (E524), hydrochloric acid (E507)) - Presence before IVT of the following symptoms: ocular redness, burning sensation, corneal pathology, headache.
DOES THE RESEARCH INCLUDE PEOPLE WITH NO CONDITION?	☒No ☐ yes

	All people included are people who have an appointment for an Intra Vitreous Injection (IVT)
PERSONAL RECRUITMENT PROCEDURES	All patients who made an appointment for an Intra Vitreous Injection (IVT) at the IOO Jules Verne during the recruitment period.
INFORMATION AND TRACEABILITY PROCEDURES FOR NON-OPPOSITION	**Patient information** Patients will be fully and fairly informed, in understandable terms, of the objectives of the study, the nature of the information collected, and their right to object at any time to the use of the data collected. All this information appears on an information form given to patients during their preoperative consultation. Patients will be informed of the following: - Presentation of the research project - The nature of the information that will be used for this research - The recipient of the data In accordance to European Regulation No. 2016/679/EU of April 27, 2016 (applicable from May 25, 2018) and the amended "Computers and Liberty" law of January 6, 1978, the patient benefits from the following rights: - Right of access, rectification, portability and erasure of their data - Right to limit the processing of their data For legitimate reasons, the right to oppose the processing of data concerning them **Collection not opposed** Patients will have to stipulate if they agree that we use their answers to the questionnaires

DISADVANTAGES FOR PEOPLE INCLUDED IN THE RESEARCH	The answers to a questionnaire during an IVT do not present a risk for the patient. Evaluation of our current practice using a questionnaire
DESCRIPTION OF THE DIFFERENT ANESTHETIC EYE DROPS USED DURING IVT	**<u>TETRACAINE 1 PER CENT THEA, eye drops in solution in single-dose container</u> Tetracaine Hydrochloride**[25] Eye drops in solution, contains an active substance, Tetracaine®. This substance is a local anesthetic capable of penetrating certain parts of the eye such as the cornea and the conjunctiva. This drug is indicated as a local anesthetic during various surgical procedures or various eye examinations. The side effects listed below are from post-marketing experience with tetracaine. Since these effects were reported spontaneously by a population of indeterminate size, it is not possible to estimate their frequency precisely, which is therefore considered to be indeterminate. - **Immune system disorders** Hypersensitivity including erythema, pruritus. - **Eye conditions** Keratitis (including ulcerative keratitis), corneal erosion, corneal oedema, eye irritation, eye pain. . **<u>OXYBUPROCAINE THEA HYDROCHLORIDE 1.6mg/0.4ml, eye drops in a single-dose container</u> Oxybuprocaine Hydrochloride** [26] Ophthalmic local anesthetic

	Like all medicines, this medicine can cause side effects, although not everyone gets them. - A few collapses with bradycardia have been exceptionally reported - Possibility of transient tingling or irritation upon instillation. **<u>OPHTESIC 20 mg/g, ophthalmic gel in single-dose container</u> lidocaine hydrochloride**[27] OPHTESIC is an anesthetic ophthalmic gel used during ophthalmic procedures. According to the public drug database, the following side effects of lidocaine gel have been described with an unknown frequency: - Conjunctival redness, changes in corneal epithelium, eye burning sensation, pitted corneal inflammation, corneal swelling
EXPECTED DURATION OF DATA COLLECTION BY INTERVIEW OR QUESTIONNAIRE FOR A PARTICIPANT	The duration of the interview is estimated at: 5-10 minutes for each questionnaire.
TOTAL FORECAST DURATION OF RESEARCH PARTICIPATION FOR A PARTICIPANT IF DATA COLLECTION IS CARRIED OUT SEVERAL TIMES	- 5-10 minutes for the 1st assessment - 5-10 minutes for the 2nd assessment

MAXIMUM ESTIMATED TRANSPORT TIME FOR PARTICIPANTS	no transportation 1st questionnaire: the day of the IVT 2nd questionnaire: the day of the IVT
MAXIMUM ESTIMATED TRANSPORT TIME FOR PARTICIPANTS	no transportation 1st questionnaire: the day of the consultation, IVT or surgery 2nd questionnaire carried out: if the patient had a VAS score greater than or equal to 4 and switched to the so-called improved anesthesia protocol with lidocaine gel
NAME AND CONTACT DETAILS OF THE DATA PROTECTION OFFICER	**Last name First Name : BOSC François** Address: Jules Verne West Ophthalmological Institute Clinical Research Department 2-4 route de Paris - 44300 NANTES Email: f.bosc@ophtalliance.fr

OphtAlliance

RELATED TREATMENTS TO DATA OF PERSONS CONCERNED BYRESEARCHES

Pursuant to Article 5, paragraph 1, point c of the GDPR, the data processed must be adequate, relevant, and limited to what is strictly necessary in relation to the purposes of the processing. In this respect, the data controller undertakes to collect only the data strictly necessary and relevant to the objectives of the research..

DATA PERSONAL ORIGIN

The data relating to the persons lending themselves to research will come exclusively from the interested parties themselves.

ARE SENSITIVE DATA PROCESSED?

The collection of certain data, particularly sensitive, is strictly regulated by the GDPR and requires special vigilance. These are data revealing the alleged racial or ethnic origin, political opinions, religious or philosophical beliefs or trade union membership of individuals, genetic and biometric data, data concerning health, sex life or sexual orientation of persons, data relating to criminal convictions or offenses, as well as the unique national identification number (NIR or social security number).

☐ YES ☒ NO

If so why ? :

DATA COLLECTED CATEGORIES

The data demographic

- Pseudo-anonymized data: one number per patient

Exclusion: surname, first name, registration number in the national identification directory natural persons)

- Age (Only the year of birth will be collected to get the age)
- Sex

Clinical data

- □ □1Number of prior IVTs (< 3 | | ; 4 to 10 | | ; > 11 | |)
- □ □2Injected product
- □ □3Pathology requiring the injection
- □ □4Needle gauge for IVT
- □ □5Dial in which the IVT is carried out
- □ □6Anesthetic
- □ □7Eye treatments
- □ □8allergies
- □ □9History of eye surgeries
- □ □10Oral pain medication: ☐YES ☐ NO

The answers to the questionnaires

- <u>The answers to questionnaire 1:</u>
  - □ HAD Anxiety Scale (Hospital Anxiety and Depression Scale - Authors: AS Zigmond and RP Snaith - French translation JL Lépine)
  - □ Measurement of pain intensity at the time of placement of the**blepharostat**: EVA scale (1 to 10)
  - □ Measurement of pain intensity at the time of injection: EVA scale (1 to10)

- <u>The answers to questionnaire number 2</u>(for patients who experienced asignificant pain (EVA > 4)

- HAD Anxiety Scale (Hospital Anxiety and Depression Scale - Authors: AS Zigmond and RP Snaith - French translation JL Lépine)
- Measurement of pain intensityat the time of placement of the blepharostat: EVA scale (1 to 10)
- Measurement of pain intensityat the time of injection: EVA scale (1 to 10)
- Measure of pain relief: simple verbal scale (0 to 4)

DATA RECIPIENTS CATEGORIES

Internal recipients

Jean-François Le Rouic: Ophthalmologist	Principal investigator
Charlotte Clemenceau: Nurse	Responsible for : - Administration of questionnaires
Sophie Dupouy: TEC nurse	Responsible for : - Perform data entry (epidata software)
Sandra Delaunay: ARC Orthoptist	Responsible for : - Responsible for controlling data entry
Héloïse De Neuville: CRA nurse	Responsible for : - Administration of questionnaires
Marie-Lou Charles: ARC Orthoptist	Responsible for : - Make the entrydata (epidata software)
Anne Barrucand: biostatistician	Responsible for : - Perform statistical analysis

External recipients *(e.g. funder, subsidiaries, partners, etc.)*

Study carried out internally

Transfers of data outside the EU: is personal data transferred outside the European Union?

☐ YES ☒ NO

If so, to which country (ies)? :

In specific situations (transfer to a third country not covered by an adequacy decision of the European Commission, and without the guarantees mentioned in Articles 46 and 47 of the GDPR), specific guarantees must be provided for and documented in theregister (Article 49 of the GDPR). Consult the CNIL website

No external data transfer will not be carried out, research is conducted internally. Its purpose is to answer the questions of Ophtalliance doctors who wish to evaluate their current practice.

SECURITY MEASURES

The data will be protected according to the General Data Protection Regulation GDPR.

Access to the data will be under the responsibility of the data controller: Dr JF Le Rouic

DATA CONFIDENTIALITY

In accordance with the legislative provisions in force (ArticlesL.1121-3 and R.5121-13 of the Public Health Code), persons having direct access to source data will take all necessary precautions to ensure the confidentiality of information relating to persons who agree to it. and in particular with regard to their identity as well as to results obtained. These people, like the doctors themselves, are subject to professional secrecy.

During the research or at its end, the data collected on the people who agree to it and transmitted to the promoter by the doctors (or any other specialized contributors) will be made pseudo-anonymous. Under no circumstances will they clearly show the names of the persons concerned or their addresses:

- Number to identify patients

- Only the year of birth is collected
- no address
- No phone number
- No social security number

DATA ENTRY AND PROCESSING

Data entry into a spreadsheet will be done by

- The CRA: Marie-Lou Charles
- The TEC nurse: Sophie Dupouy

They will be responsible for data entry from the answers to the questionnaires on a spreadsheet.

The data will be protected according to the General Data Protection Regulation (GDPR). The patient's references will therefore be pseudo-anonymized: only a patient number will appear in the spreadsheet

Sandra Delaunay, ARC orthoptist will be responsible for monitoring and verifying:

- The collection of non-objection from patients
- Compliance with inclusion and exclusion criteria
- Compliance with Good Clinical Practices
- The quality and integrity of the data collected, any missing data

Then she will send the spreadsheet in csv format (spreadsheet with only the patient numbers) to Anne Barrucand, the biostatistician in charge of the statistical analysis.

Anne Barrucand will not have access to the patient name/number correspondence table nor to the data source.

The data management of the study database will be carried out using the R version software 3.4.4 (R-project) by the biostatistician Anne Barrucand in order to verify the consistency of the information. If the check highlights certain errors, Sandra Delaunay will be in charge of verifying the information in the source data.

Once the verification process is complete, the freezing of the database will be decided in a concerted manner between the promoter (SELARL Ophtalliance), the investigator (Dr. JF Le Rouic) and the biostatistician (A. Barrucand)

DATA SECURITY

The data will be protected according to the General Data Protection Regulation GDPR.

Access to the data will be under the responsibility of the data controller: Dr JF Le Rouic

He will be the only one to keep the table of correspondence between the coded identity of the participant in the search and its name.

The data controller as well as the persons as well as the following persons:

- Jean-François Le Rouic: Ophthalmologist
- Sophie Dupouy: TEC nurse
- Sandra Delaunay: ARC Orthoptist
- Héloïse De Neuville: CRA nurse
- Marie Lou Charles: ARC Orthoptist
- Charlotte Clemenceau : Nurse

are the only persons authorized to access the data of patients who did not opposed to participating in the research.

The people mentioned above are certified: Good Clinical Practice ICH E6.

IT SECURITY

The spreadsheet and computer data will be stored on a clinic server that has an ISO 27000 standard for computer security.

Workstation anti-virus: Kaspersky Endpoint Security for Window 11.1.1.126

Individual password to access the computerized data files with a list of authorized persons restricted to the 6 persons mentioned above.

Server secured by login + password

PAPER DATA SECURITY

The premises of the Jules Verne clinic have:

- From an alarm
- Locking of all offices
- From a security post
- Anti-fire device: Fire door, smoke detector

DATA CATEGORIES STORAGE TIME

The following documents will be archived by the name of the study in the premises of the service of the Jules Verne clinic from the beginning of the study until the end of the period of practical usefulness

These documents are:

- The summary of the study
- Information forms and original signed non-objection collections
- Individual data (authenticated copies of raw data)
- Statistical analyzes
- Final report of the study

At the end of the period of practical usefulness, all the documents to be archived at the Jules Verne clinic and will be kept under the responsibility of Héloïse de Neuville for 3 years after the end of the study in accordance with institutional practices.

No displacement or destruction can be carried out without the agreement of the Promoter (Ophtalliance SELARL). At the end of the 3 years, the promoter will be consulted for destruction. All data, documents and reports are subject to audit or inspection.

AUDIT AND INSPECTION

An audit carried out at the request of the sponsor or an inspection carried out by the health authorities may be carried out at any time by persons independent of those responsible for the research. Its objective is to ensure the quality of research, the validity of its results and compliance with the law and regulations in force.

Auditors/inspectors should have direct access to source and medical data and any useful document related to the conduct of the clinical study.

The confidentiality of the data and the anonymity of the subjects will then be respected.

Investigators agree to abide by the Sponsor's requirements and the authority competent with regard to a research audit or inspection.

The audit may apply to all stages of the research, from the development of the protocol to the publication of the results and the classification of the data used or produced within the framework of the research.

CERTIFICATE

I hereby certify on behalf of the promoter (SELARL Ophtalliance) that the research entitled: Study of Anesthesia by Lidocaine Gel for IntrA vitreous injections, whose principal investigator is Dr JF Le Rouic is designed and carried out in accordance with the legal and regulatory provisions of "Decree No. 2017-884 of May 9, 2017 modifying certain regulatory provisions relating to research involving humans"

Done in Nantes on June 03, 2022

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