PROTOCOL FOR A RETROSPECTIVE STUDY

Efficacy and safety evaluation of MONOBLUE DUAL View and MONOBLUE ILM View vital stains during vitrectomy surgery

NewBlueDyes

Version number: v 6 – **Date** 5/07/2022

Internal ref. nbr: S65841

Sponsor

University Hospitals Leuven (UZ Leuven)

Herestraat 49, B-3000 Leuven

Coordinating Investigator

Prof. Dr. Peter Stalmans

LIST OF PARTICIPATING SITES

NA

Confidentiality Statement

The information in this document is strictly confidential and is available for review to Investigators, potential Investigators and appropriate Ethics Committees, Institutional Review Boards or Competent Authorities. No disclosure should take place without written authorization from the Sponsor

SIGNATURES

Title: Efficacy and safety evaluation of MONOBLUE DUAL View and MONOBLUE ILM View vital stains during vitrectomy surgery

Protocol: NewBlueDyes

The undersigned confirm that the above referenced protocol has been acknowledged and accepted, they agree to conduct the Study in compliance with the approved protocol, and will adhere to: the ICH guidelines, the most recent version of the Declaration of Helsinki, the EU General Data Protection Regulation 2016/679 (GDPR), relevant Belgian laws implementing the GDPR, the Belgian Law of August 22nd 2002 on patient rights, and any other regulatory requirements and Standard Operating Procedures (SOPs), as applicable.

The undersigned agree not to disclose the confidential information contained in this document for any purpose other than the evaluation or conduct of the Study, without prior written consent of the Sponsor.

Principal Investigator

Prof. Dr. Peter Stalmans

.....	.....	.....
Name & Title	Signature	Date

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LIST OF ABBREVIATIONS

Abbreviation	**Definition**

(e)CRF	(electronic) Case Report Form
CI	Coordinating Investigator
DPA	Data Processing Annex
DTA	Data Transfer Agreement
EC	Ethics Committee
EU	European Union
GCP	Good Clinical Practice (latest version of ICH E6)
GDPR	General Data Protection Regulation
ICH	International Conference on Harmonisation
JCI	Joint Commission International
PI	Principal Investigator (Participating Site)
SOP	Standard Operating Procedure
BBG	Brilliant Blue G
BCVA	Best Corrected Visual Acuity
DC	Declaration of Conformity
ERM	Epiretinal Membrane(s)
ICG	Indocyanine Green
IFU	Instruction For Use
ILM	Inner Limiting Membrane
KWS	Klinisch Werkstation (EMR used in UZLeuven)
PEG	Poly-Ethylene Glycol
PBS	Phosphate Buffer Saline
PVR	Proliferative vitreoretinopathy
RPE	Retinal Pigment Epithelial cells
TB	Trypan Blue
EMR	Electronical Medical Record
MDR	Medical Device Regulation
NA	Not applicable

FUNDING AND SUPPORT

Funder	Type of Financial or Non-Financial Support
Arcad/BVI	grant

ROLES AND RESPONSIBILITIES

The Principle Investigator (PI) is responsible for the conduct of the Study at his/her Participating Site, and for protecting the rights, safety and well-being of Study participants. As such the PI must ensure adequate supervision of the Study conduct at the Participating Site. If any tasks are delegated, the PI will maintain a log of appropriately qualified persons to whom he/she has delegated specified Study-related duties. The PI will ensure that adequate training is provided and documented for all Study staff, prior to conducting assigned Study-related activities. Even when certain activities are delegated, the PI will ultimately remain responsible for the conduct of the Study at his/her Participating Site.

It is the Coordinating Investigator's (CI's) responsibility to supervise the general conduct (e.g. Study progress, communication, protocol training and support of the participating sites, annual reporting to the Ethics Committee (EC), end of Study notification(s) and results reporting…) of the Study. The CI fulfils both Investigator and Sponsor responsibilities, as outlined in International Conference on Harmonisation – Good Clinical Practice (ICH-GCP) E6(R2) and applicable regulations.

PI and CI shall each be referred to as «Investigator(s)».

STUDY SYNOPSIS

Title of clinical Study («Study»)	Efficacy and safety evaluation of MONOBLUE DUAL View and MONOBLUE ILM View vital stains during vitrectomy surgery
Protocol Short Title Acronym	NewBlueDyes
Sponsor name	University Hospitals Leuven (UZ Leuven)>
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Coordinating Investigator	NA
Medical devices	Monoblue Dual View Monoblue ILM View
Study rationale	Retrospective Data Collection
Primary objective	Efficacy: visualization of membranes stained based on binary subjective evaluation.

Secondary objective(s)	• Efficacy: subjective assessment of surgical help provided by the product
	• Safety:
	  ○ Rate and severity of potential study-related products adverse events
	  ○ Visual outcome at the last postoperative visit

Endpoints	**Effectiveness Outcomes**: Improvement in BCVA after 2 months as compared to preoperative BVCVA. **Safety Outcomes:** Safety will be assessed based on incidence and severity of investigational device-related adverse events.
Time frame of collecting data for retrospective analysis	SEPTEMBER 2021-APRIL 2022

1 Background and Rationale

Retinal surgery was first performed in the 1960-ies when Charles Schepens developed the technique of scleral buckling using indirect ophthalmoscopy. Later on, pars plana vitrectomy was developed by pioneering surgeons such as Robert Machemer and Relja Zivojinovic. The latter surgical technique became widely adopted in the 1980-ies.
During vitrectomy surgery, there is often the need to remove tissue from the neural retina:

- Epiretinal membranes (ERM): newly formed tissue from dedifferentiated retinal pigment epithelial (RPE) cells. These membranes typically are observed in the following diseases:
    - Macular pucker: formation of fibrosis over the macula, most frequently seen after the formation of posterior vitreous detachment.
    - Proliferative vitreoretinopathy (PVR): formation of fibrotic scars mostly in the (mid)periphery of the retina, most frequently seen in long-standing retinal detachment and after previous retinal surgery.
- Inner Limiting Membrane (ILM): the most inner layer of the retina, formed by the basal membranes of the Müller cells. The removal of this ILM is required to treat different diseases of the retina:
    - Macular hole
    - Vitreomacular traction
    - Macular edema
    - Also, in case of surgery for removal of macular pucker or PVR, concomitant removal of the ILM is frequently performed to avoid re-growth of these membranes.

ERM and ILM are both transparent tissues, similar to the neural retina. Hence, it is not that easy to remove ERM and ILM without touching (and damaging) the underlying neural retina. For this purpose, vital dyes have been developed to selectively stain the tissues that need be removed without staining the underlying neural retina.
The first dye used (off-label) to stain the ILM was Indocyanine Green (ICG), but several reports of toxicity after using that dye have been published. Hence, its used is nowadays mostly abandoned.
Shortly thereafter, Trypan Blue (TB) was introduced to stain ERM. Till today, this dye is used on-label and available from different manufacturers. TB is commercialized in a 0.06% concentration to stain the lens capsule and in a 0.15% concentration to stain ERM. Although TB has good staining properties of ERM, it induces only minimal staining of the ILM.
A few years later, Brilliant Blue G (BBG) was commercialized to selectively stain ILM, and is today still the golden standard for ILM staining. BBG offers a good and selective staining of the ILM, and is a rather transparent solution, hence the surgeon can see the surface of the retina during the surgery. However, BBG hardly stains the ERM.
The first commercial TB and BBG vital dyes were dissolved in BSS, hence had the same gravity as the BSS used to infuse the eye during vitrectomy surgery. As a result, when injecting a 'cloud' of the vital dye, it was difficult for the dye to reach and color specifically the desired retinal tissue. In newer commercial products, the dyes are dissolved in a heavier-than-water dissolvent (such as poly-ethylene glycol: PEG), which makes them sink down to the retinal surface when injected in the vitreous cavity during surgery.

Since it is frequently necessary to remove both ILM and ERM during vitrectomy surgery, solutions that combine TB and BBG are now also available.
In UZLeuven, two types of vital stains are being used during vitrectomy surgery:

- BBG 0,025 % dissolved in PEG (ILM Blue® – DORC): when only ILM peeling is required.
- BBG 0,025 % + TB 0.15% dissolved in PEG (Membrane Blue Dual® – DORC): when either ERM removal is required, or combination of ERM + ILM removal.

More recently, two new staining dyes were commercialized by ARCADOPHTA:

- Monoblue ILM View: DDG 0.025 % dissolved in PBS (phosphate buffer saline) with 2.6% diglycerol. DDG is a triphenylmethane dye with a chemical formula: $C_{46}H_{46}N_3Na0_7S_2$ and a molecular weight of 840 Dalton. This dye is used to stain the ILM, similar as ILM Blue. The diglycerol makes it heavier than water to optimize the contact between the dye and the retina, similar as ILM Blue.
- Monoblue Dual View: DDG 0.025 % and Trypan Blue 0.09% dissolved in PBS with 2.6% diglycerol, which is used the same way as Membrane Blue Dual.

In laboratory and ex vivo tests, it was shown that both dyes have the following properties:

- Monoblue ILM view:
    - It stains ILM as good as ILM Blue.
    - It is heavier than water, hence sinks down to the retinal surface.

Monoblue Dual View

- Monoblue Dual View may offer better transparency to see the retinal surface during surgery compared to Membrane Blue Dual.
- It has a lower concentration of TB, but is still expected to stain ERM as effectively as Membrane Blue Dual, but with a potential better safety profile since its lower concentration.

Both above mentioned dye solutions were CE marked on April 22, 2021 by ARCADOPHTA, located 11 rue Antoine Ricord, Toulouse, France, known as the legal manufacturer (see to CE certificate and Declaration of Conformity (DC) provided herewith in **Appendix 1A, 1B, 1C**).
We obtained approval from the CMM UZLeuven to perform a demo with these products. For this purpose, samples of Monoblue ILM View and Monoblue Dual View were obtained from the manufacturer.

Study products:
This clinical study is a post-marketing clinical follow-up study of two medical devices: Monoblue ILM View and Monoblue Dual View, legally marketed in EU by the company Arcadophta, and to be conducted in accordance to the provisions of the respective IFU (instructions for use) provided in **Appendix 2**).

Intended Use:
The products are intended for use as an aid during vitrectomy procedure in adult that will undergo a vitreoretinal surgery.
Monoblue ILM View is indicated for staining of the Internal Limiting Membrane (ILM)
Monoblue Dual View is indicated for staining of ILM and ERM (Epiretinal Membrane).

Study population
The study population consists of adult patients with retinal conditions requiring peeling of ILM and/or ERM

Mechanism of action
MONOBLUE-ILM VIEW and MONOBLUE-Dual View are staining solutions for the posterior eye segment. They are intended to be applied directly to the areas of the membranes to be removed and color all parts of the membrane with which they come into contact, without penetrating these membranes.

2 Study Objectives and Design

2.1 Study objectives

To determine efficacy and safety of MONOBLUE DUAL View and MONOBLUE ILM View (study products) vital stains during vitrectomy surgery
Both study products are CE-marked and legally marketed in Europe. The data collection will serve as Post-Marketing Clinical Follow-up according MDR provisions. Retrospective data will also be collected for the two reference products: ILM Blue® (DORC) and Membrane Blue Dual® (DORC) to serve as control. For this purpose, patient data will be used that were collected in studies S61408 (Comparative study 23G vs 27G vitrectomy), S63610 (Comparative study 27G vitrectomy vs larger gauge surgery) and S64913 (EVA Nexus Field Observation Study).
The expected effect of the study products is to provide the retinal surgeon with adequate aid in visualizing the membranes involved in the retinal pathology to treat, thanks to their staining capabilities. The performance of the study products is related to the visualization of retinal tissues (ILM and/or ERM) during the vitrectomy procedure, when these tissues cannot be distinguished accurately enough without staining. Their use allows for better identification of these tissues and facilitates their removal by the surgeon. The clinical benefit of using ophthalmic dyes is to increase the patient's ability to recover anatomically and functionally by allowing more precise surgery with an effective visualization tool.
Along with collecting post-marketing clinical follow-up data on the subject products, the outcomes of the present study results may be used at the UZLeuven Hospital to decide to use Monoblue ILM View and/or Monoblue Dual View as standard-of-care, replacing Membrane Blue Dual and ILM Blue.

2.2 Primary Endpoints

Efficacy: visualization of membranes stained based on binary subjective evaluation.
Assessment of efficacy (success) is provided in section 3, Study Endpoints.

2.3 Secondary Endpoints

- Efficacy: subjective assessment of surgical help provided by the product
- Safety:
    - Rate and severity of potential study-related products adverse events
    - Visual outcome at the last postoperative visit

The study hypothesis to be verified is non-inferiority in term of efficacy between study products and comparator based on a binary subjective evaluation of visualization of membranes stained. The proportion of success between study products and comparator will be studied, covariates (age, gender, visual acuity in the affected eye, surgery type being vitrectomy or phaco plus vitrectomy) taken into using a propensity score methodology.

2.4 Time frame of the retrospective analysis

SEPTEMBER 2021 – APRIL 2022

3 Study Population / Eligibility Criteria

3.1 Inclusion criteria

Participants eligible for inclusion in this Study must meet **all** of the following criteria:

Adult patients who underwent for vitrectomy surgery where ILM and/or ERM removal is required:

- Macular holes (ILM staining)
- Macular pucker (ILM and ERM staining)
- Vitreomacular traction (ILM staining)

3.2 Exclusion criteria

Participants eligible for this Study must **not** meet any of the following criteria:

- Children aged <18 years
- Vitrectomy for other indication than mentioned in 3.1
- Patients that have concomitant eye disease that may influence the outcome of the surgery, e.g. terminal glaucoma
- Patients that did to comply to the postoperative examination visit 6-10 weeks after the surgery

4 Statistics and Data Analysis

The primary outcome of the study is the success of the products based on assessment of efficacy of the staining dye.
Safety of the dye will be assessed by comparing the surgical outcome of the patients to a similar control group that underwent surgery using the staining dyes presently used in our department (see study endpoints).

Statistical analyses will be performed with R version 3.6.2 or higher. In case of missing values, the underlying missingness process (MCAR, MAR or MNAR) will be investigated and 15 multiple imputations will be performed using the **MICE** R package.
We will test with the statistical test of Jamshidian and Jalal (2010), implemented in the MissMech R Package (Jamshidian, Jalal & Jansen,2014), whether missing data were MCAR. If they were not MCAR, we investigated whether or not the missing mechanism could be explained by baseline characteristics (eg, sociodemographic, medical features) of patients using logistic regression, which would suggest an MAR mechanism. If missing data were not MCAR or MAR, they were considered as MNAR
For each dataset created,two propensity scores will be performed: a first one between the Monoblue ILM View and the ILM Blue, and a second one between the Monoblue Dual View and Membrane Blue Dual. The next covariates were selected for the propensity score: age, gender, visual acuity of the affected eye, surgery type of the affected eye (vitrectomy only vs phaco and vitrectomy)). The Covariate Balancing Propensity Score provided in the R CBPS package (Imai & Ratkovic, 2014) will used to estimate an Average Treatment Effect (ATE). The ATE will be estimated by covariate balancing and requesting an exact match. An absolute standardized difference less than 10–15% will be considered to support the assumption of balance between the groups. Unlike the P-value, this method is not affected by the sample size, and it could be used to compare the relative balance of variables that were measured in different units (Austin, 2011). Results (obtained after matching) will be expressed as the mean and standard deviation (SD) for continuous variables or the percentage for categorical variables. The survey R package will be used to perform linear regressions for continuous outcome variables and logistic regressions for binary variable. These regressions

will include the treatment group effect, the weight resulting from the matching, and variables present in the propensity score. This procedure will provide a doubly-robust estimator, which corrected the last remaining possible imbalance between the covariates and produced an unbiased treatment effect (Funk et al., 2010). We will then combine results of the 15 regressions by taking the mean of the estimates of the regression coefficients of the treatment effect and theits associated p-value for each imputed dataser (the so-called, 'MIte approach'), as described by Leyrat et al. (2019). Adjusted P-values less than 0.05 will considered significant.

Bibliography:

Austin P. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res 2011;46:399–424.

Funk MJ, Westreich D, Wiesen C, Sturmer T, Brookhart MA, Davidian M. Doubly robust estimation of causal effects. Am J Epidemiol 2010;173:761–7.

Imai, K., and Ratkovic, M. Covariate Balancing Propensity Score. Journal of the Royal Statistical Society, Series B, 2014;76, 243–263

Jamshidian M, Jalal S. Tests of homoscedasticity, normality, and missing completely at random for incomplete multivariate data. *Psychometrika*. 2010;75:649–674.

Jamshidian M, Jalal S, Jansen C. MissMech: an R package for testing homoscedasticity, multivariate normality, and missing completely at random (MCAR). *J Stat Software*. 2014;56:1–31.

Leyrat, C., Seaman, S. R., White, I.R., Douglas, I., Smeeth, L., Kim, J., Resche-Rigon, M., Carpenter, J.R. & Williamson, E.J. (2019). Propensity score analysis with partially observed covariates: how should multiple imputation be used? Statistical Methods in Medical Research, 28(1), 3-19.

5 Data handling

5.1 General data handling information

Data collection, handling, processing and transfer for the purpose of this Study will be performed in compliance with applicable regulations, guidelines for clinical studies and internal procedures. It remains the responsibility of the Investigator to check that all data relating to the Study, as specified in the Study protocol, are entered into the electronic Case Report Form ((e)CRF) in accordance with the instructions provided and that the forms are filled out accurately, completely and in a timely manner.

(e)CRFs are provided by the Sponsor for each participant. The Study data will be transcribed from the source records into an (e)CRF by Study Staff.

The (e)CRFs shall under no circumstances capture personal data such as but not limited to the participant or their relative(s) name, home address, contact details, full date of birth medical record number (e.g. UZ Leuven EAD number), social security number etc.

Transfer of the pseudonymized data will be performed via a secured method of transfer taking into account all applicable security arrangements and regulations (such as the European General Data Protection Regulation). The receiving party will be bound by contractual agreement to keep the transferred data confidential at all times and to only process the data for the purpose of the Study. To this end, appropriate Data Transfer Agreements (DTAs) will be established.

5.2 Study specific data handling information

The data will be stored in a secure RedCap database on the UZ Leuven, and will only be accessible to specific persons: Prof. Dr. Peter Stalmans, the CTA Ingeborg Vriens and possible monitors from the CTC, if required. Data will be stored for a period of 20 years.

KWS will be used to capture study related data.

The following data will be collected in the (e)CRF :

Primary endpoint:Study product efficacy (success, defined as follows:

From the surgical report, the following data will be extracted:

1. In case of surgery for macular hole or vitreomacular traction:
    - A. Was the staining of the ILM satisfactory to initiate the peeling: yes / no
    - B. Was the staining of the ILM satisfactory to create the ILM rhexis: yes / no
    - C. Was it necessary to use another vital dye in order to obtain satisfactory staining: yes / no

Success is defined as answer "yes" to 1.A and/or 1.B

2. In case of surgery for macular pucker:
    - A. Was the staining of the ERM satisfactory for its removal: yes / no
    - B. In case the ILM was removed separately from the ERM:
        - i. Was the staining of the ILM satisfactory to initiate the peeling: yes / no
        - ii. Was the staining of the ILM satisfactory to create the ILM rhexis: yes / no
    - C. Was MONOBLUE DUAL View repeatedly injected: yes / no
    - D. Was it necessary to use another vital dye in order to remove the ERM: yes / no
    - E. Was it necessary to use another vital dye in order to remove the ILM: yes / no

Success is defined as "yes" answer to 2.A and 2B.i or 2Bii

Secondary endpoint: assessment of surgical safety

The following endpoints will be used to determine surgical safety:

- Occurrence of adverse events during or after the surgery, whereby both treatment groups will be compared to the corresponding control groups (see above). Occurrence of adverse events will be collected over the duration of the study and up to week 6-10 postoperative, and will be assessed cumulatively.
- Visual outcome at the last postoperative visit, i.e. week 6-10 after the surgery

6 Ethical and Regulatory Considerations

6.1 Ethics Committee (EC) review & reports

Before the start of the Study, this protocol and other related documents will be submitted for review to the EC for Study authorization. The Study shall not commence until such approvals have been obtained and until other relevant essential Study documents, such as duly signed contract agreements, evidence of adequate Study financing etc. are in place.

6.2 Protocol / GCP compliance

The Study must be performed in accordance with the protocol, current ICH and ICH-GCP guidelines, and applicable regulatory and country-specific requirements. ICH guidelines are an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the

participation of human participants. Compliance with this standard provides public assurance that the rights, safety, and well-being of Study participants are protected, consistent with the principles that originated in the most recent version of the Declaration of Helsinki, and that the Study data are credible, reliable and reproducible.

6.3 Data protection and participant confidentiality

The Study will be conducted in compliance with the requirements of the EU General Data Protection Regulation 2016/679 (GDPR), and the relevant Belgian laws implementing the GDPR including the Belgian Privacy Act of 30 July 2018 on the protection of privacy in relation to the processing of personal data. Any collection, processing and disclosure of personal data, such as participant health and medical information is subject to compliance with the aforementioned personal data protection laws.

Any personal data shall be treated as confidential at all times including during collection, handling and use or processing, and the personal data (including in any electronic format) shall be stored securely at all times and with all technical and organizational security measures that would be necessary for compliance with EU and national data protection legislation (whichever is more stringent). The Sponsor shall take appropriate measures to ensure the security of all personal data and guard against unauthorized access thereto or disclosure thereof or loss or destruction while in its custody.

7 Research Registration, Dissemination of Results and Publication Policy

The Declaration of Helsinki (latest version) and European and Belgian regulations require that every research Study involving human participants be registered in a publicly accessible database before recruitment of the first participant. The CI is responsible for registering the Study.

In addition, the CI will fulfil their ethical obligation to disseminate and make the research results publicly available. As such the CI is accountable for the timeliness, completeness and accuracy of the reports. Researchers, authors, Sponsors, editors and publishers must adhere to accepted guidelines for ethical reporting. Negative and inconclusive, as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in publication.

8 Joint Commission International (JCI)

In order to ensure the same quality and safety standards in patient care for clinical research as commonly applied by the Sponsor in its regular activities, and in accordance with JCI standards, the Sponsor shall comply with the following obligations: (a) the Sponsor will use trained and qualified employees or contractors to manage and coordinate the Study; (b) the Sponsor will ensure that multi-center Study reporting is reliable and valid, statistically accurate, ethical, and unbiased. (c) the Sponsor will not grant incentives, other than standard compensations and reimbursement of costs, to Study participants or to participating site's staff that would compromise the integrity of the research; (d) the Sponsor is responsible for monitoring and evaluating the quality, safety, and ethics of the Study and will respect the participating site's policies and processes when performing such monitoring and evaluation activities; (e) the Sponsor will protect the privacy and confidentiality of the Study participants in accordance with all applicable laws.

9 References

1. Ocular toxicity study of trypan blue injected into the vitreous cavity of rabbit eyes. Veckeneer M, van Overdam K, Monzer J, Kobuch K, van Marle W, Spekreijse H, van Meurs J. Graefes Arch Clin Exp Ophthalmol. 2001 Sep;239(9):698-704.
2. Double vital staining using trypan blue and infracyanine green in macular pucker surgery. Stalmans P, Feron EJ, Parys-Van Ginderdeuren R, Van Lommel A, Melles GR, Veckeneer M. Br J Ophthalmol. 2003 Jun;87(6):713-6.
3. Trypan blue staining of epiretinal membranes in proliferative vitreoretinopathy. Feron EJ, Veckeneer M, Parys-Van Ginderdeuren R, Van Lommel A, Melles GR, Stalmans P. Arch Ophthalmol. 2002 Feb;120(2):141-4.
4. Retinal damage from indocyanine green in experimental macular surgery. Gandorfer A, Haritoglou C, Gandorfer A, Kampik A. Invest Ophthalmol Vis Sci. 2003.
5. Toxicity of indocyanine green in vitreoretinal surgery. Gandorfer A, Haritoglou C, Kampik A. Dev Ophthalmol. 2008;42:69-81.
6. Trypan blue staining in vitreoretinal surgery. Teba FA, Mohr A, Eckardt C, Wong D, Kusaka S, Joondeph BC, Feron EJ, Stalmans P, Van Overdam K, Melles GR. Ophthalmology. 2003 Dec;110(12):2409-12.
7. Retinal toxicity of indocyanine green in albino rabbits. Goldstein M, Zemel E, Loewenstein A, Perlman I. Invest Ophthalmol Vis Sci. 2006 May;47(5):2100-7.
8. Trypan blue not toxic for retinal pigment epithelium in vitro. Stalmans P, Van Aken EH, Melles G, Veckeneer M, Feron EJ, Stalmans I. Am J Ophthalmol. 2003 Feb;135(2):234-6.
9. Which colour suits the vitreoretinal surgeon? Collaer N, Stalmans P. Br J Ophthalmol. 2007 Sep;91(9):1101-2.
10. Brilliant Blue G as protective agent against trypan blue toxicity in human retinal pigment epithelial cells in vitro. Awad D, Schrader I, Bartok M, Sudumbrekar N, Mohr A, Gabel D. Graefes Arch Clin Exp Ophthalmol. 2013 Jul;251(7):1735-40.
11. Dyes for Eyes™: hydrodynamics, biocompatibility and efficacy of 'heavy' (dual) dyes for chromovitrectomy. Mohr A, Bruinsma M, Oellerich S, Frank H, Gabel D, Melles GR; International Chromovitrectomy Collaboration. Ophthalmologica. 2013;230 Suppl 2:51-8.
12. Novel 'heavy' dyes for retinal membrane staining during macular surgery: multicenter clinical assessment. Veckeneer M, Mohr A, Alharthi E, Azad R, Bashshur ZF, Bertelli E, Bejjani RA, Bouassida B, Bourla D, Crespo IC, Fahed C, Fayyad F, Mura M, Nawrocki J, Rivett K, Scharioth GB, Shkvorchenko DO, Szurman P, Van Wijck H, Wong IY, Wong DS, Frank J, Oellerich S, Bruinsma M, Melles GR. Acta Ophthalmol. 2014 Jun;92(4):339-44.
13. Toxicity and phototoxicity in human ARPE-19 retinal pigment epithelium cells of dyes commonly used in retinal surgery. Awad D, Wilińska J, Gousia D, Shi X, Eddous J, Müller A, Wagner V, Hillner C, Brannath W, Mohr A, Gabel D. Eur J Ophthalmol. 2018 Jul;28(4):433-440.
14. Vital stains for vitreoretinal surgery. Veckeneer M, Stalmans P. Retina. 2013 Apr;33(4):673-7.
15. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. Duker JS, Kaiser PK, Binder S, de Smet MD, Gaudric A, Reichel E, Sadda SR, Sebag J, Spaide RF, Stalmans P. Ophthalmology. 2013 Dec;120(12):2611-2619.
16. Oct-based interpretation of the vitreomacular interface and indications for pharmacologic vitreolysis. Stalmans P, Duker JS, Kaiser PK, Heier JS, Dugel PU, Gandorfer A, Sebag J, Haller JA. Retina. 2013 Nov-Dec;33(10):2003-11.
17. Optic nerve atrophy after vitrectomy with indocyanine green-assisted internal limiting membrane peeling in diffuse diabetic macular edema. Ando F, Yasui O, Hirose H & Ohba N. Graefes Arch Clin Exp Ophthalmol (2004): 242: 995-999.