

ICR.net European Network of Clinical Research in Ophthalmology Information Update – June 2017

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#### **EVICR.net Activities – Update 2017**

EVICR.net – the European Vision Institute Clinical Research Network – is a network of European Ophthalmological Clinical Research Sites, dedicated to perform multinational clinical research in ophthalmology with the highest standards of quality, following the European, International Regulations for Clinical Research and ICH-GCP Guidelines.

EVICR.net's aim is to strengthen the capacity of the European Union to perform multinational clinical research studies to develop and optimise the use of diagnostic, prevention and treatment strategies in ophthalmology, contributing to bring better patient care to daily clinical practice.

EVICR.net offers a unique platform for ophthalmology multinational clinical research in Europe and a useful industry resource in order to contribute to the development of new drugs, medical devices and biomarkers.

*AIBILI*, in Coimbra, Portugal, is the headquarters and Coordinating Centre of EVICR.net.

At present, EVICR.net has 105 Clinical Ophthalmological Centres members from 18 European countries (Table 1; Fig. 1). The Network has coordinated already 14 studies and has at present 9 multinational clinical studies ongoing of which 3 are European Union-funded projects (Table 2).

Any clinical research site in ophthalmology can apply for EVICR.net membership. In order to become a member, basic requirements need to be fulfilled, such as adequate facilities to perform clinical research studies, qualified and experienced personnel, experience in multinational clinical studies and implementation of organizational Standard Operating Procedures (SOPs) according to ICH-GCP Guidelines.

EVICR.net aims to be a much needed resource for the coordination of multinational investigator-initiated research (IIR) particularly when applying for EU funding or industry IIR grants. Scientifically, it is organized by ophthalmology subspecialties Expert Committees, namely: Age-Related Macular Degeneration; Retinal Dystrophies; Diabetic Retinopathy and Vascular Diseases; Glaucoma; Anterior Segment; and Ocular Surface, Inflammation, Dry Eye and Allergies. It also has Transversal Sections dedicated to Reading Centres, Rare Diseases and Medical Devices.

### **Aims and Objectives**

The main aims and objectives of EVICR.net are to:

- offer logistical support for investigator-initiated research (IIR) within the European Union;
- guarantee a high level of quality and excellence in eye clinical research performed by its members according to ICH-GCP Guidelines;
- coordinate training activities for its members;
- promote educational programs on clinical trial research in ophthalmology;
- serve as a resource for industry in performing multinational clinical research in ophthalmology;
- promote quality, transparency and optimal use of clinical research data;
- communicate with patients and citizens and be a source of information for challenges and opportunities raised by clinical research in ophthalmology.

#### **Organization (Fig. 2)**

The *General Assembly* consists of all EVICR.net members (one representative per Clinical Site) and is the supreme organ of the Network.

The *Steering Committee* is responsible for the activities of the EVICR.net and acts as its decision-making body within the framework set by the General Assembly. The Steering Committee consists of the Chairman, the Coordinator of each Expert Committee and Transversal Section and the CEO of the Coordinating Centre.

The *Expert Committees* and *Transversal Sections* have a fundamental role in the scientific organization of EVICR.net and cover the main ophthalmological research areas.

The *Industry Advisory Board* advises the Steering Committee in all matters of strategic relevance, particularly pertaining collaborations with industry. The Industry Advisory Board is composed of individuals or representatives of companies that have committed support for the activities of EVICR.net. The members of the Industry Advisory Board are Alcon, Allergan, Bayer, Novartis, Pfizer, Roche, Santen and Théa.

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Fig. 1. Number of members per country.

**Table 1.** Number of members per country

Austria	1	
Belgium	3	
Denmark	2	
Finland	1	
France	13	
Germany	16	
Greece	1	
Ireland	1	
Israel	3	
Italy	10	
Poland	1	
Portugal	15	
Slovakei	1	
Slovenia	1	
Spain	16	
Switzerland	6	
The Netherlands	5	
United Kingdom	9	
Total	105	

The *Coordinating Centre, AIBILI*, is the single contact point for the members and industry when performing multinational ophthalmological clinical research in Europe. Annually, the Coordinating Centre updates the EVICR.net Research Resources Directory where all members have their resources listed, namely: staff, equipment and facilities as well as their scientific areas of clinical research and their five most relevant publications. All members have access to a restricted area in the website that is also kept updated by the Coordinating Centre. The Coordinating Centre is responsible for the certification of EVICR.net Clinical Site Members.

### **Clinical Studies and Registries**

The EVICR.net Coordinating Centre assumes the coordination and management of IIR in ophthalmology across Europe through the Network. EVICR.net members have the opportunity to participate in IIR within the Network as well as to submit abstracts for IIR in order to be evaluated by a specific Expert Committee. When approved, they will have access to support in coordinating and implementing the IIR.

# Multinational Clinical Research Studies under EVICR.net (2010–2017) (Fig. 3)

EVICR.net IIR has been growing in the last years, giving the opportunity for investigators to perform multinational clinical research of high quality in compliance with ICH-GCP Guidelines assuming that the rights, safety and wellbeing of the trial subjects are protected and that the clinical data are credible. EVICR.net has contributed to the improvement of diagnostic, prevention and treatment strategies in ophthalmology.

# Standard Operating Procedures – Quality Assurance System

EVICR.net has developed a quality system for its members compliant with ICH-GCP Guidelines. It provides for free to its members 9 Organizational Standard Operating Procedures (SOPs). All our Clinical Sites Members agree to adopt these SOPs in their centres which will be checked before they are certified as Sites of Excellence.

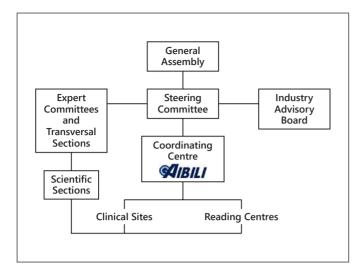
The implementation of these 9 Organizational SOPs will permit the Clinical Sites to have a standard way of working in compliance with ICH-GCP Guidelines when performing clinical research.

EVICR.net has also developed 31 Technical SOPs for performing specific ophthalmic examinations or evaluations that can be used within the Network for clinical studies. These SOPs are also made available to the members.

In parallel, EVICR.net has developed 22 Organizational SOPs for the Reading Centres so they can work as a network of Reading Centres and be able to have the capacity to respond to the industry needs for grading ophthalmological images in a standardised way with the most novel equipments.

### **EVICR.net Annual Members Meeting**

The 11th Annual Members Meeting took place on November 9–10, 2016, in Antwerp, Belgium, and was hosted by Prof. Marie-Jose Tassignon from CS12. The meeting was attended by 93 participants representing 42 Clinical Sites and Industry Advisory Board Members from Alcon-Novartis, Allergan, Bayer and Santen. Dr. Lee Jampol from the Diabetic Retinopathy Clinical Research Network – DRCR.net (USA) was an invited Speaker in or-



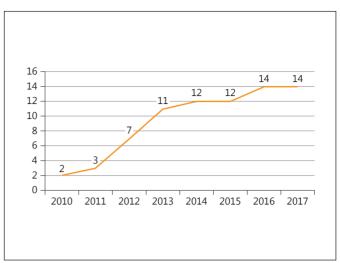


Fig. 2. Organization.

Fig. 3. Number of multinational clinical research studies.

Ongoing clinical research	Area of subspecialty						
	AMD	retinal dystrophies	diabetic retinopathy and retinal vascular disease	glaucoma	anterior segment	ocular surface, inflammation, dry eye and allergies	
Clinical trials (IIR)	ATLANTIC <sup>b</sup> MACUSTAR <sup>a, c</sup>	IRD Genetic Study <sup>c</sup>	EUROCONDOR <sup>a</sup> PROTEUS <sup>b</sup> ARTES <sup>b</sup>	STRONG <sup>a</sup>	REDCAKE <sup>d</sup>		
Registries (industry)			IRISS				
Total (9)	2	1	4	1	1	0	

der to foster the collaboration of EVICR.net Diabetic Retinopathy Section and DRCR.net in clinical research.

The 12th EVICR.net Annual Members Meeting will take place on October 19–20, 2017, in Giessen, Germany, and will be hosted by Prof. Birgit Lorenz from CS65.

### Collaboration with ECRIN – European Clinical Research Infrastructure Network

EVICR.net, as a disease-oriented network in ophthalmology, has been accepted and registered as an ECRIN-ERIC affiliate partner. ECRIN-ERIC is the European Clinical Research Infrastructure Network that supports the conduct of independent, multinational clinical trials by managing and supporting clinical trials across borders, connecting networks, and advising and implementing policy, competitiveness and integration in European clinical research.

EVICR.net provides scientific and medical expertise, access to patients and research infrastructure for multinational clinical research in vision and ophthalmology.

### Collaboration with DRCR.net – Diabetic Retinopathy Clinical Research Network

A research collaboration is now developed with DRCR.net (USA). This collaboration will be initiated through genetic studies in Diabetic Retinopathy.

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## European Reference Network on Rare Eye Diseases (ERN-EYE)

H. Dollfus (Strasbourg, France) leads the European Reference Network (ERN) on Rare Eye Diseases composed of 29 healthcare providers from 13 European countries. EVICR.net is a member of the Scientific, Medical and Ethical Advisory Board (SMEAB). ERN-EYE is organized in thematic groups: Retinal; Neuro-Ophthalmology; Paediatric and Anterior Segment.

EVICR.net collaborates with ERN-EYE through the Rare Diseases Transversal Section (B. Lorenz) for Ophthalmology Technical SOPs (by subspecialties) and experience with Quality Systems and certification of Clinical Sites as well as by providing overall management and logistical support needed in future multinational investigator initiated studies in rare eye diseases.

### **Translational Network in Ophthalmology**

EVICR.net has been challenged by the European Medicines Agency (EMA) to identify within EVICR.net Clinical Research Centres that are interested in translational research. EMA identified a gap in the early stages of research and is working with EVICR.net as a pilot interaction model in ophthalmology.

### Ocular Surface, Inflammation, Dry Eye and Allergies Capacities

Since this new Expert Committee installation, on Ocular Surface, Inflammation, Dry Eye and Allergies Capacities, a questionnaire was sent to all EVICR.net Centres to identify their interest in this new section. Responses were received from 49 Clinical Sites.

### **Alliances and Partnerships**

EVICR.net has established preferred alliances with two CROs, AppleTree (Switzerland) and Eurotrials (Portugal), to perform independent evaluation visits of the Clinical Sites for the EVICR.net Clinical Site certification process when needed.

Collaborations have also been established with other CROs, namely with Covance, Parexel and Quintiles, to perform feasibility assessments for potential multinational clinical research in ophthalmology.

# EVICR.net – European Network of Clinical Research in Ophthalmology

*Chairman (2013–2017)* Jose Sahel, MD, PhD

Steering Committee (2016–2019)

Francesco Bandello, MD, PhD – AMD Expert Committee Coordinator

Hendrik Scholl, MD, PhD – Retinal Dystrophies Expert Committee Coordinator

José Cunha-Vaz, MD, PhD – Diabetic Retinopathy and Vascular Diseases Expert Committee Coordinator

Francesca Cordeiro, MD, PhD – Glaucoma Expert Committee Coordinator

Marie-José Tassignon, MD, PhD – Anterior Segment Expert Committee Coordinator

Marc D. de Smet, MD, PhD – Ocular Surface, Inflammation, Dry Eye and Allergies Expert Committee Coordinator

Tunde Peto, MD, PhD, FHCO, FHCD – Reading Centres Transversal Section Coordinator

Jorge Alió, MD, PhD – Medical Devices Transversal Section Coordinator

Birgit Lorenz, MD, PhD – Rare Diseases Transversal Section Coordinator

Cecília Martinho, BSc - CEO, Coordinating Centre (AIBILI)

Contacts

EVICR.net

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### Multinational Clinical Research Studies per Subspecialty

- 1. Age-Related Macular Degeneration
- 1.1 Ongoing Studies
- 1 AMD8 ECR-AMD-2015–09 ATLANTIC A randomized, double-masked, sham-controlled phase 4 study of the efficacy, safety and tolerability of intravitreal aflibercept monotherapy compared to aflibercept with adjunctive photodynamic therapy in patients with polypoidal choroidal vasculopathy. CI: R. Silva. IIR grant from Bayer. Ongoing.
- 2 MACUSTAR Development of novel clinical endpoints for interventional clinical trials with a regulatory and patient access intention in patients with intermediate age-related macular degeneration (AMD). CI: F. Holz (CS 15). Project approved by IMI2. *In contracting phase. Project scheduled to start in September 2017 – 5 years.*

2. Retinal Dystrophies

2.1 Contacts from Industry

1 IRD Genetic Study – EVICR.net CC was contacted by Spark Therapeutics, a company with focus on gene therapies, for cooperation and to be responsible for the inherited retinal disorder (IRD) initiative diseases in Europe as they have already started in the USA. CI: H. Scholl (CS110). In contracting phase.

*3. Diabetic Retinopathy and Vascular Diseases 3.1 Ongoing Studies* 

1 DR4 – ECR-RET-2011–03 – EUROCONDOR – FP7-Health2011–278040–2. PI: J. Cunha-Vaz (CS 1). LPLV: October 2015. Final study report expected to be concluded by June 2017 by BCN Peptides. *Ongoing*.

Martinho/Fernandes

- 2 DR5 ECR-RET-2013–05 PROTEUS Prospective, randomized, multicenter, open label, phase II/III study to assess efficacy and safety of ranibizumab 0.5 mg intravitreal injections plus panretinal photocoagulation (PRP) versus and PRP in monotherapy in the treatment of patients with high-risk proliferative diabetic retinopathy. CI: J. Figueira (CS 01). IIR grant from Novartis. Final Report issued 28/11/2016. *Pending publication*.
- 3 DR6 ECR-RET-2014-07 ARTES A collaborative retrospective trial on the efficacy and safety of intravitreal dexamethasone implant (Ozurdex) in patients with diabetic macular edema (DME). The European DME Registrar Study. CI: A. Loewenstein (CS 60). IIR grant from Allergan. *Final report expected to be issued in mid-2017.*
- 4 ECR-ICT-11 IRISS An open-label registry study of the safety of Iluvien<sup>®</sup> (fluocinolone acetonide 190 μg intravitreal implant in applicator) – Alimera. Ongoing.

4. Glaucoma

4.1 Ongoing Studies

 G4–ECR-GLC-2012–04–STRONG–FP7-Health2012–305321. CI: N. Pfeiffer (CS 2). EU project coordinated by N. Pfeiffer (CS 2), involves the CC, other EVICR.net Clinical Sites and the SME GeneSignal. *Ongoing*.

5. Anterior Segment

5.1 Ongoing Studies

1 C6 – The Retrospective Keratoconus Progression Study – RED-CAKE. CI: J. Rozema (CS 12). Application to the Flemish grant approved. *CS 12 in contracting phase.* 

### **Publication and Dissemination**

### Studies

Progressive visibility of EVICR.net activities from EVICR.net studies.

- ECR-ICT-09 LHON
- EVER 2014 (poster)
- ECR-RET-2010-02 RET02
- ARVO 2014 Congress (poster)
- ARVO 2015 Congress (poster)
- IOVS 2015;56:5698-5705
- Ophthalmic Res 2015;54:112–117
- Ophthalmic Res 2015;54:118–123
- Ophthalmic Res 2015;55:19–25
- IOVS (in revision)
- ECR-RET-2011-03 EUROCONDOR
- Br J Ophthalmol 2012;96:1285–1290
- Trends Endocrinol Metab 2014;25:23–33
- IOVS 2015;56:1802
- Ophthalmic Res 2017;57:107–117
- Diabetes; Baseline results (in revision)
- ECR-GLC-2013-06 SPORT
- Graefes Arch Clin Exp Ophthalmol 2016;254:1151–1158.
- ECR-CCRS-2010-01 Project Gullstrand
  - Cahier de Ophtalmologie 2013;170;40-42
  - Optom Vis Sci 2014;91:1–10
  - IOVS 2015;56:7029–35
  - BMC Ophthalmol 2016;16:79

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## List of EVICR.net Members (per Country)

<i>Austria (1)</i> CS No. 19:	Medical University of Vienna, Department of Ophthalmology, Vienna	CS No. 5:	Faculty of Medicine Mannheim of the Ruprecht-Karls-University Heidelberg, Department of Ophthalmology, Mannheim
<i>Belgium (3)</i> CS No. 8:	Ghent University Hospital, Department of	CS No. 9:	University Hospital Tübingen (UKT), STZ Biomed & STZ Eyetrial, Center for
	Ophthalmology, Ghent	CS No. 11:	Ophthalmology, Tübingen University Eye Hospital Munich, Munich
CS No. 12:	Antwerp University Hospital, Department of Ophthalmology, Antwerp	CS No. 15:	University of Bonn, Department of Ophthalmology, Bonn
CS No. 18:	University Hospitals Leuven, Department of Ophthalmology, Leuven	CS No. 21:	University Medical Center Hamburg-Eppendorf, Department of
Denmark (2)			Ophthalmology, Hamburg
CS No. 30:	Rigshospitalet – Glostrup, Department of Ophthalmology, Copenhagen University,	CS No. 24:	University of Freiburg, Department of Ophthalmology, Freiburg
	Glostrup	CS No. 27:	University Eye Hospital, Leipzig
CS No. 73:	Odense University Hospital, Department of Ophthalmology, Odense	CS No. 43:	RWTH Aachen University, Department of Ophthalmology, Aachen
<i>Finland (1)</i>	Demostra ant of Onlythelmede are Kusania	CS No. 44:	University Eye Clinic, Center for Vision Science, Bochum
CS No. 91:	Department of Ophthalmology, Kuopio University Hospital, Kuopio	CS No. 54:	University of Düsseldorf, Department of Ophthalmology, Düsseldorf
France (13)		CS No. 56:	University of Heidelberg, International Vision
CS No. 3:	Centre Hospitalier Creteil, University Eye Clinic, Paris		Correction Research Centre (IVCRC), Heidelberg
CS No. 6:	Centre National d'Ophthalmologie des Quinze-Vingts, Centre d'Investigation	CS No. 65:	Justus-Liebig-University Giessen, Department of Ophthalmology, Giessen
CS No. 13:	Clinique, Paris CHU Gabriel Montpied, Unité de Recherche	CS No. 77:	Universität zu Köln, Zentrum für Augenheilkunde, Cologne
C3 N0, 15:	Clinique, Service d'Ophtalmologie,	CS No. 111:	Department of Ophthalmology, University of Münster Medical Center, Münster
CS No. 14:	Clermont-Ferrand Hôpital Lariboisière, Department of Ophthalmology, Paris	CS No. 115:	Department of Ophthalmology, St. Franziskus-Hospital, Münster
CS No. 42:	University Hospital, CHU Dijon, Department of Ophthalmology, Dijon	Greece (1)	
CS No. 48:	CLAIROP – Centre Loco-Regional de l'AP-HP Necker pour l'Innovation et la Recherche en Ophtalmologie Pediatrique, Paris	CS No. 71:	Laboratory of Research and Clinical Applications in Ophthalmology, Aristotle University of Thessaloniki, 1st Department of Ophthalmology, AHEPA University Hospital, Thessaloniki
CS No. 61:	CHU Pellegrin, Service Ophtalmologie, Bordeaux	Ireland (1)	
CS No. 86:	Centre Hospitalier Universitaire Amiens- Picardie, Service d'Ophtalmologie, Amiens	CS No. 31:	Mater Vision Institute (MVI), Dublin
CS No. 92:	Clinical Trial Unit, Department of	<i>Israel (3)</i> CS No. 60:	Tel Aviv Sourasky Medical Center,
	Ophthalmology, CHU Nord, Aix Marseille University, Marseille		Department of Ophthalmology, Tel Aviv
CS No. 93:	Department of Ophthalmology, Centre Hospitalier Henri Duffaut, Avignon	CS No. 88:	Kaplan Medical Center, Ophthalmology Department, Rehovot
CS No. 97:	Centre Ophtalmologique de l'Odeon, Paris	CS No. 100:	Meir Medical Center, Kfar-Saba
CS No. 99:	Department of Ophthalmology, Croix Rousse University Hospital, Lyon	<i>Italy (10)</i> CS No. 16:	University of Milan, Centre for Clinical Trials
CS No. 113:	Service d'Ophtalmologie, Hôpital		at San Paolo Hospital, Milan
	Pitié-Salpêtrière, Paris	CS No. 20:	G.B. Bietti Foundation – IRCCS, Rome
Germany (16)		CS No. 34:	Luigi Sacco Hospital, University of Milan, Department of Ophthalmology Milan
CS No. 2:	University Medical Center, Johannes Gutenberg University, Department of Ophthalmology, Mainz	CS No. 36:	Department of Ophthalmology, Milan Catholic University, Institute of Ophthalmology, Rome

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	Ophthalmology, Center for Clinical Trials,
	Padua
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	Ophthalmology, Udine
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	Excellence Eye Research Centre, Chieti
CS No. 64:	Ophthalmic Research Unit, Department of
	Basic Medical Sciences, Neuroscience and
	Sense Organs, Bari
CS No. 67:	University Vita Salute – Scientific Institute of
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	Milan
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CS No. 17:	Department of Ophthalmology, Radboud
	University Medical Centre, Nijmegen
CS No. 25:	Academic Medical Center, Department of
	Ophthalmology, Amsterdam
CS No. 40:	Rotterdam Eye Hospital, Rotterdam
CS No. 76:	University Eye Clinic, Maastricht
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CS No. 117:	APDP – Diabetes Portugal, Lisbon
Slovakia (1)	
CS No. 87:	Department of Ophthalmology, University Hospital, Comenius University, Bratislava
01 : (1)	± '
Slovenia (1)	II. in a to Madical Contrast (I is blives
CS No. 23:	University Medical Centre of Ljubljana, University Eye Hospital, Ljubljana
Spain (16)	
CS No. 7:	Vissum Corporación Oftalmológica Alicante, Alicante
CS No. 26:	Centro de Oftalmología Barraquer, Barcelona
CS No. 38:	Institut Català de Retina (ICR), Clinical Trial Unit, Barcelona
CS No. 41:	Centro Médico Teknon, Institut de la Màcula i
	de la Retina, Barcelona
CS No. 51:	Fundación para la Investigacion Biomedica y Sanitaria (FISABIO) – Oftalmología Médica, Valencia
CS No. 52:	Universitary Hospital Josep Trueta of Girona,
05 110. 52.	Department of Ophthalmology, Girona
CS No. 74:	Hospital Vall d'Hebrón, Department of
00110.71	Ophthalmology, Barcelona
CS No. 75:	Vallés Oftalmologia Research, Barcelona
CS No. 78:	Instituto Oftalmológico Fernández-Vega,
C5 110. 78.	Oviedo
CS No. 89:	Dos de Maig Hospital, Ophthalmology Department, Barcelona
CS No. 95:	Instituto de Microcirugia Ocular, Barcelona
CS No. 96:	Ophthalmology Department, Hospital de LaPaz, Madrid
CS No. 98:	Servicio Oftalmología, Hospital Universitario y Politécnico de la Fe, Valencia
CS No. 105:	Unidad Clínica de Retina – Servicio de Oftalmología, Complejo Hospitalario
	Universitario de Albacete, Albacete
CS No. 109:	Department of Ophthalmology Fundación
	Jiménez Díaz University Hospital, Madrid
CS No. 116:	Retina Unit, Department of Ophthalmology, Bellvitge University Hospital, L'Hospitalet de
0 1 1 1 ( - )	Llobregat
<i>Switzerland (6)</i>	x 1 . 1 x
CS No. 22:	Inselspital, University of Bern, Department of Ophthalmology, Bern
CS No. 49:	Jules Gonin Eye Hospital, Fondation Asile des
CS No. 95	Aveugles, Lausanne
CS No. 85:	Clinical Research Centre, Mémorial A. de Rothschild, Geneva
CS No. 108:	MIOS SA, Lausanne
CS No. 110:	University Hospital Basel, University Eye
	Clinic, Basel
CS No. 112:	Department of Ophthalmology, University Hospital Zurich, Zurich

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