CLINICAL TRIALS

GIMSO

GRUPO DE INVESTIGACIÓN E INNOVACIÓN
MIGUEL SERVET OFTALMOLOGÍA

ÍNDICE

DEFINITION

All research conducted on humans to determine or confirm clinical effects, and/or other pharmacodynamic effects, and/or to detect adverse reactions, and/or study the absorption, distribution, metabolism and excretion of one or more drugs under investigation in order to determine their safety and efficacy.

ETHICS IN CLINICAL TRIALS

The Helsinki Declaration is the most important document in the ethics of research involving human subjects. Adopted by the 18th World Medical Assembly in Helsinki (Finland) in June 1964, it states that the doctor must protect the life, health, dignity, integrity, right to self-determination, privacy and confidentiality of the personal information of patients involved in research.

Participation of individuals in clinical trials should always be subject to their ability to consent in a free and voluntary way.

Informed consent involves a document that the patient signs voluntarily, accepting inclusion in the clinical trial by means of a positive act of decision involving altruism within society.

The Ethics Research Committee (ERC) is an independent, multidisciplinary body composed of healthcare professionals and lay members, whose purpose is to ensure the protection of the rights, safety and well-being of subjects participating in any biomedical research project.

The ERC must evaluate methodological, ethical and legal aspects of the projects prior to issuing an favorable judgement allowing the commencement of a clinical trial.

When the project reaches the researcher, having been sanctioned by the legal and ethical filter of the ERC, the researcher becomes the ultimate ethical filter, and with his knowledge of good clinical practices, and in compliance with the principles of "respect for persons, beneficence and justice" (Belmont Report, 1979), the clinical trial can be undertaken according to professional experience. All researchers in any one trial must be trained in good clinical practices and they should know and apply research ethics. Likewise, they have to complete numerous training sessions prior to the execution of each clinical trial.

COMPONENTS OF A CLINICAL TRIAL

- The Sponsor: The sponsor of a clinical trial is the individual, company, institution or organization who has possession of the initial idea of the particular clinical trial. The sponsor is responsible for the initiation, management and/or financing of the clinical trial.
- Trial monitors or CRAs (Clinical Research Associates): professionals in the field of health who develop activities related to medical research, mainly in the management and monitoring of clinical trials. Their work is based on their knowledge of all the aspects of a clinical trial, and in ensuring that each of the centers participating in the trial are familiar with the relevant protocols, they carry out their work in accordance with the requirements of the test protocol, good clinical practice and applicable legislation.
- Protocol: The protocol is the document that contains all the information on the design, methodology and organization for conducting the clinical trial.

PHASES OF CLINICAL TRIALS

The development of new drugs follows a series of stages (phases I-IV), which begin once the molecule has been synthesized, biological tests have been performed and animal studies have been completed.

- PHASE I
  The aim here is to define the optimal dose, to demonstrate its safety and tolerability, to define the toxicity profile and to establish the pharmacokinetic characteristics of the research product.

- PHASE II
  The objective of this phase is to determine the efficacy of the product, establish the dose-response relationship and to further enhance the safety data obtained in phase I.

- PHASE III
  In this phase the intention is to evaluate the safety and efficacy of the treatment in conditions similar to those in future administration of the product under investigation in the general population, so the sample of subjects is broader. The drug will be compared with standard preestablished treatments, if any, or with a placebo if there are none.

- PHASE IV
  Consists of monitoring the drug once it has been licensed and marketed, in search of long-term efficacy and safety.

CONFIDENTIALITY IN CLINICAL TRIALS

"Whatsoever I shall see or hear in the course of my profession, as well as outside my profession in my intercourse with men, if it be what should not be published abroad, I will never divulge, holding such things to be holy secrets." (Hippocratic Oath 500 BC).

In medical research the measures aimed at protecting the privacy of subjects participating in a clinical trial, is known as **confidentiality**.

Researchers responsible for studies have a duty of confidentiality, that is to say they must not divulge personal information about a subject to anyone outside of the trial without specific permission from the subject.

There are several methods that the researcher can employ to maintain confidentiality, for example using special codes to identify participants and maintaining a limited number of staff with access to such information.

Likewise, it is the responsibility of the **Ethics Committee** to monitor that, in each study there are conditions that ensure confidentiality of information of trial participants. In this regard, the Committee assesses, prior to the commencement of the project, that the researcher uses informed consent, specifies what information will be collected, who will have access to it, and what measures will be taken to protect such information throughout the trial and henceforth after the trial has been completed.

During the development of the project, the ethics committee ensures that the established conditions are fulfilled so that information is kept secure.

TEAM COMPOSITION OF A CLINICAL TRIAL

In the Ophthalmology service of Miguel Servet University Hospital we have undertaken clinical trials for more than 20 years.

The areas in which these have been performed are in Glaucoma, Retina and Ocular Surface.

The clinical trials team consists of a structured group of highly qualified professionals specifically chosen for the development of a particular trial.

The constituent figures of each project are:

- **Principal Researcher:** Has utmost responsibility for the correct execution of the trial.
- **Sub-researchers:** Professionals in charge of performing consultations with patients according to protocol and fulfilling the ethical precepts.
- **Data manager:** Technician in charge of additional tests and data management.

AUDITS AND INSPECTIONS

The execution of clinical trials is subject to continuous audit and/or periodic inspections in the centers where the trials are undertaken.

An **audit** consists of an independent, comprehensive and systematic review of activities and documentation, in order to assess whether such activities were implemented in accordance with the protocol, standard work procedures, standards of good clinical practice and valid legislation.

Similarly, an **inspection** is an official review undertaken by a competent responsible authority (e.g. FDA- The regulatory body for the administration of medicines and foods in the United States) of all related elements within the trial.

These authorities are bodies responsible for the protection of public health by means of the regulation of medicinal products for human and veterinary use, vaccines and other biological products, medical devices, food standards, cosmetics, dietary supplements and radiation-emitting products.

In our long history of conducting clinical trials, we have successfully undergone numerous audits and inspections.

CURRENTLY ACTIVE CLINICAL TRIALS

Over the last 5 years, about 20 clinical trials have been performed simultaneously in our ophthalmology service. Currently, these are the Active Clinical Trials in the different areas of Glaucoma, Retina and Ocular Surface.

GLAUCOMA AREA

SPONSOR	TRIAL NAME	PROTOCOL CODE	
IVANTIS	HYDRUS 3	CP-10-002	A prospective randomized multicenter trial comparing the Hydrus Aqueus implant with the IStent™ to lower intraocular pressure in glaucoma patients undergoing cataract surgery (Hydrus III).
IVANTIS	HYDRUS 4	CP-11-001	Safety and efficacy of the Hydrus™ aqueous implant to reduce intraocular pressure in glaucoma patients undergoing cataract surgery. A prospective, multicenter, randomized controlled trial (Hydrus4 study).
IVANTIS	HYDRUS 5	CP-12-001 HYDRUS V	Prospective, multicenter and randomized comparison of Hydrus™ with IStent™ to reduce intraocular pressure in primary open-angle glaucoma.
IVANTIS	HYDRUS 7	CP-16-001 HYDRUS VII	The Hydrus microstent for refractory open-angle glaucoma: a prospective, multicenter clinical trial.
Allergan	ARTEMIS	192024-091	Efficacy and safety of slow-release Bimatoprost in patients with open-angle glaucoma or ocular hypertension.
Neurim PHARMACEUTICALS	PIROMELATINA	Piromelatine-IOP1	Randomized, double-blind, placebo-controlled study of oral therapy with pyromelatin in patients with ocular hypertension (HTO) or with primary open-angle glaucoma (APAG).
aerie Pharmaceuticals, Inc.	MERCURY - 3	Mercury - 3	A prospective, double-masked, randomized, multicenter, active comparator with parallel groups of 6 months duration to evaluate the safety and efficacy of ocular hypotensive agent PG324 ophthalmic solution compared to GANFORT® (bimatoprost 0.03% / timolol 0.5%) ophthalmic solution in subjects with elevated intraocular pressure (MERCURY 3)
NOVARTIS	GLJ576-P001	Protocol Training QVJ499A2402	Multicenter, randomized, masked study. Double and parallel groups to demonstrate the reducing effect of IOP with 1% brinzolamide/0.2% brimonidine (administered twice daily) when added to the 0.004% travoprost/0.5% timolol solution In subjects with open-angle glaucoma or ocular hypertension.

CURRENTLY ACTIVE CLINICAL TRIALS

RETINA AREA

SPONSOR	TRIAL NAME	PROTOCOL CODE	
Alcon A Novartis Division	HARRIER	RTH258-C002	Two-year, randomized, double-blind, multicenter, two-group study comparing efficacy and safety of RTH258 6mg compared to Aflibercept in subjects with exudative age-related macular degeneration.
Allergan	CEDAR	1509998-005	Safety and efficacy of Abicipar Pegol (AGN-150998) in patients with neovascular age-related macular degeneration.
bioeq	COLUMBUS	FYB201-C2015-01-P3	Efficacy and Safety of Biosimilar Ranibizumab FYB201 in Comparison to Lucentis in patients with neovascular age-related macular degeneration.
BAYER	ARIES	BAY86-5321/17508	Treatment of neovascular age-related macular degeneration (NVAMD) over 2 years with a standard of treatment and extension (T+E) of 2 mg intravitreal Aflibercept injection (IAI). Randomized, open, controlled study with active substance and parallel groups in stage IV/IIIb (ARIES study).
Genentech A Member of the Roche Group	TULIP	TG-MV-017	Use of Intravitreal JETREA® in Clinical Practice: A European Prospective Drug Utilisation Study - See more at: http://www.hra.nhs.uk/news/research-summaries/jetrea-drug-utilisation-study-tulip-tg-mv-017/#sthash.UCq4CzVA.dpuf
NOVARTIS	OBTAIN	CRFB002F2401	A 36 month observational study to describe the long-term efficacy and safety of ranibizumab 0.5 mg treatment in patients with visual impairment due to choroidal neovascularization (CNV) secondary to pathologic myopia (PM).
LABORATORIOS Thea	RETILUT	Mercury - 3	Multicenter, randomized, human nutritional supplementation study in patients with unilateral wet AMD.

CURRENTLY ACTIVE CLINICAL TRIALS

OCULAR SURFACE AREA

SPONSOR	TRIAL NAME	PROTOCOL CODE	
mc2 biotek	PAD-Ciclo	MC-03-C1	A phase II, multicenter, randomized, double-masked, 4 paralle armas, controlled 6-month trial designed to evaluate the safety and efficacy of PAD Coclisporin (CsA 0.06& and 0.03%) ophthalmic dispersion administered once daily in combination with lubricant therapy and a 3-month post treatment safety follow-up in moderate to severe dry eye patients.
LABORATORIOS Thea	CACICOL	LT40-20-302	Performance and safety assessment of T4020 combined with standard post-operative therapy versus satandard post-operative therapy in managing corneal epithelial defect following epi-off accelerated corneal crosslinking.
AVX PHARMA	AVIZOREX	AVX012-CT-001	A phase I/II double-blind, placebo-controlled study assessing the safety and efficacy of AVX-012 ophthalmic solution in subjects with mild to moderate dry eye syndrome.
sylentis	HELIX	S33E1601 / SYL1001_IV: Helix/ Sylentis	A double-masked study of SYL1001 in patients with moderate to severe dry eye disease (DED).

RESEARCHERS

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