The Hillingdon Hospitals NHS
NHS Foundation Trust

Ophthalmology Research and Development

Portfolio of Studies

Research Team Contact Details

Research Consultant

Ms Sheena George — Sheena.George@nhs.net

Research Coordinators

Kash Khuttan — Kash.Khuttan@thh.nhs.uk

Dean Kenward-Miller — Dean.Kenward-Miller@nhs.net

General Enquiries — 01895 279771

Contents

SPECTRI

Long Title:
A phase III, multicenter, randomized, double-masked, sham-controlled study to assess the efficacy and safety of Lampalizumab administered intravitreally to patients with Geographic Atrophy secondary to Age-Related Macular Degeneration

Sponsor:	Roche
Start Recruitment:	16th June 2015
End Recruitment:	
Duration of Study:	100 weeks
Number of patients to be recruited:	6

Inclusion Criteria

Patients must meet the following criteria for study entry:

a) General Inclusion Criteria

• Willingness to provide signed informed consent. Additionally, at U.S. sites, patients must provide Health Insurance Portability and Accountability Act (HIPAA) authorization, and in other countries, as applicable according to national laws.

• Age ≥50 years

• For women who are not postmenopausal (≥12 months of non-therapy-induced amenorrhea) or surgically sterile (absence of ovaries and/or uterus): agreement to remain abstinent or use single or combined contraceptive methods that result in a failure rate of <1% per year during the treatment period and for at least 30 (±7) days after the last dose of study treatment. Abstinence is only acceptable if it is in line with the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not acceptable methods of contraception.

Sexually active men will be required to use a barrier contraceptive method (condom), even if they have been surgically sterilized, for the duration of the treatment period and for at least 30 (±7) days after the last dose of study treatment.

• Ability and willingness to undertake all scheduled visits and assessments

• Valid CFI profile biomarker result (i.e., CFI profile biomarker-positive or CFI profile biomarker-negative)

b) Ocular Inclusion Criteria: Study Eye

• BCVA of 20/100 or better (Snellen equivalent) using ETDRS charts at starting distance of 4 m

If BCVA is ≥ 20/25, at least one GA lesion must be within 250 μ m of the foveal centre

• Well demarcated area(s) of GA secondary to AMD with no evidence of prior or active CNV.

The total GA lesion size ≥2.54 mm_2 (approximately ≥1 disc area [DA]) and ≤17.78 mm_2 (approximately ≤7 DA) and must reside completely within the FAF imaging field (Field 2–30 degree image centered on the fovea). If GA is multifocal, at least 1 focal lesion must be ≥1.27 mm_2 (approximately ≥0.5 DA)

• Presence of hyperautofluorescence of either banded or diffuse patterns adjacent to the area of GA

• Sufficiently clear ocular media, adequate pupillary dilation, and fixation to permit quality fundus imaging

c) Ocular Inclusion Criteria: Non-study Eye

• GA secondary to AMD with no evidence of prior or active CNV

• GA lesion must reside completely within the FAF imaging field (Field 2–30 degree image centered on the fovea)

Exclusion Criteria

Patients who meet any of the following criteria will be excluded from study entry:

a) GA Characteristics Exclusion Criteria

- GA in either eye due to causes other than AMD (monogenetic macular dystrophies [e.g., Stargardt disease, cone rod dystrophy] or toxic maculopathies [e.g., chloroquine/hydroxychloroquine maculopathy])

b) Ocular Exclusion Criteria: Study Eye

- History of vitrectomy surgery, submacular surgery, or other surgical intervention for AMD
- Previous laser photocoagulation for CNV, diabetic macular edema, retinal vein occlusion, and proliferative diabetic retinopathy
- Prior treatment with Visudyne•, external-beam radiation therapy, or transpupillary thermotherapy
- History of prophylactic subthreshold laser treatment for AMD
- Previous intravitreal drug delivery (e.g., intravitreal corticosteroid injection, anti–angiogenic drugs, anti-complement agents, or device implantation). A single intraoperative administration of a corticosteroid during cataract surgery for cystoid macular edema prophylaxis at least 3 months prior to screening is permitted.

c) Ocular Exclusion Criteria: Non-study eye

- *Non-functioning non-study eye defined as either:*

BCVA of hand motion or worse

OR

No physical presence of non-study eye (i.e., monocular)

d) Ocular Exclusion Criteria: Both Eyes

- Previous treatment with eculizumab or participation in eculizumab studies
- Previous treatment of either eye with lampalizumab
- Previous treatment with fenretinide or participation in fenretinide studies

e) Ocular Exclusion Criteria: Concurrent Ocular Conditions

- RPE tear that involves the macula in either eye
- Any concurrent ocular or intraocular condition in the study eye (e.g., cataract or diabetic retinopathy) that, in the opinion of the investigator, could do either of the following:

Require medical or surgical intervention during the study period to prevent or treat vision loss that might result from that condition if allowed to progress untreated, could likely contribute to loss of at least two Snellen equivalent lines of BCVA during the study period

- Active uveitis and/or vitritis (grade trace or above) in either eye
- History of idiopathic or autoimmune-associated uveitis in either eye
- Active, infectious conjunctivitis, keratitis, scleritis, or endophthalmitis in either eye
- Current vitreous hemorrhage in the study eye
- History of retinal detachment or macular hole (Stage 3 or 4) in the study eye
- Aphakia or absence of the posterior capsule in the study eye
- Previous violation of the posterior capsule in the study eye unless it occurred as a result of yttrium aluminum garnet (YAG) laser posterior capsulotomy in association with prior posterior chamber intraocular lens implantation
- Spherical equivalent of the refractive error in the study eye demonstrating >8 diopters of myopia
- For patients who have undergone prior refractive or cataract surgery in the study eye, the preoperative refractive error in the study eye should not have exceeded 8 diopters of myopia.
- Intraocular surgery (including cataract surgery) in the study eye within 3 months preceding Day 1

• Uncontrolled glaucoma in the study eye (defined as intraocular pressure [IOP] ≥30 mm Hg despite treatment with anti-glaucoma medication)
• History of glaucoma-filtering surgery in the study eye
• History of corneal transplant in the study eye
• Proliferative diabetic retinopathy in either eye
• Prior or active CNV in either eye
• Central serous retinopathy in either eye
• History of recurrent infectious or inflammatory ocular disease

f) Concurrent Systemic Conditions Exclusion Criteria
• Uncontrolled blood pressure (defined as systolic >180 mm Hg and/or diastolic >110 mm Hg while patient is sitting). If a patient's initial measurement exceeds these values, a second reading may be taken 30 or more minutes later. If the patient's blood pressure must be controlled by anti-hypertensive medication, the patient can become eligible if medication is taken continuously for at least 30 days prior to Day 1.
• History of other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding that gives reasonable suspicion of a disease or condition that contraindicates the use of lampalizumab or that might affect interpretation of the results of the study or that renders the patient at high risk of treatment complications
• Treatment for active systemic infection
• Predisposition or history of increased risk of infection (i.e., history of splenectomy or chronic immunosuppression)
• Active malignancy
• History of allergy to fluorescein that is not amenable to treatment
• *History of a severe allergic reaction or anaphylactic reaction to a biologic agent or known hypersensitivity to any component of the lampalizumab injection*
• Inability to comply with study or follow-up procedures
• Inability to obtain CFP, FAF, and FA of sufficient quality to be analyzed and graded by the central reading center
• Previous participation in any studies of investigational drugs within 3 months preceding Day 1 (excluding vitamins and minerals)
• Requirement for continuous use of any medications/treatments indicated in the "Prohibited Therapy" section of the protocol
• Women who are pregnant or lactating or intending to become pregnant during the study
• Women who are not postmenopausal (≥12 months of non-therapy-induced amenorrhea) or surgically sterile must have a negative serum pregnancy test result within 21 days prior to initiation of study treatment.

LEAVO

Long Title:
A Multicentre Phase III Double-masked Randomised Controlled Non-Inferiority Trial comparing the clinical and cost effectiveness of intravitreal therapy with ranibizumab (Lucentis) vs aflibercept (Eylea) vs bevacizumab (Avastin) for Macular Oedema due to Central Retinal Vein Occlusion (CRVO).

Sponsor:	Moorfields Eye Hospital Foundation Trust
Start Recruitment:	10th June 2015
End Recruitment:	
Duration of Study:	100 weeks
Number of patients to be recruited:	8

Inclusion Criteria

1. Subjects of either sex aged ≥ 18 years.
2. Clinical diagnosis of centre-involving macular oedema (MO) due to CRVO
3. CRVO of ≤ 12 months duration.
4. Best corrected visual acuity in the study eye ≥ 19 and ≤ 73 ETDRS letters (approximate Snellen VA 3/60 to VA 6/12).
5. Best corrected visual acuity in the non-study eye ≥ 14 ETDRS letters (approximate Snellen VA ≥ 2/60).
6. SD-OCT central subfield thickness (CST) > 320μm (Spectralis) predominantly due to MO secondary to CRVO in the study eye. See appendix 1 for equivalent CST value for alternative SD-OCT machines.
7. Media clarity, pupillary dilatation and subject cooperation sufficient for adequate fundus imaging of the study eye.
8. In cases of bilateral CRVO, if both eyes are potentially eligible, unless the patient prefers otherwise the worst seeing eye will be recruited.

Exclusion Criteria

The following apply to the study eye only and to the non-study eye only where specifically stated:
1. Macular oedema considered to be due to a cause other than CRVO (e.g. diabetic macular oedema, Irvine-Gass syndrome).
2. An ocular condition is present that, in the opinion of the investigator, might affect macular oedema or alter visual acuity during the course of the study (e.g. vitreomacular traction)
3. Any previously documented diabetic retinopathy or diabetic macular oedema in the study eye.
4. Moderate or severe non proliferative diabetic retinopathy (NPDR) or quiescent, treated or active proliferative diabetic retinopathy (PDR) or macular oedema in the non-study eye. Note: Mild NPDR only is permissible in the non-study eye.
5. History of treatment for MO due to CRVO in the past 90 days with intravitreal or peribulbar corticosteroids or in the last 60 days with anti-VEGF drugs or >3 prior anti-VEGF treatments in the previous 12 months.
6. Active iris or angle neovascularisation, neovascular glaucoma, untreated NVD, NVE and vitreous haemorrhage or treatment for these conditions in the last 3 months.
7. Uncontrolled glaucoma [>30mmHg], either untreated or on anti-glaucoma medication at screening.
8. Any active periocular or intraocular infection or inflammation (e.g. conjunctivitis, keratitis, scleritis, uveitis, endophthalmitis).

Systemic exclusion criteria:

9. Uncontrolled blood pressure defined as a systolic value > 170mmHg and diastolic value > 110mmHg.
10. Myocardial infarction, stroke, transient ischaemic attack, acute congestive cardiac failure or any acute coronary event < 3 months before randomisation
11. Women of child bearing potential unless using effective methods of contraception throughout the study and for 6 months after their last injection for the trial. Effective contraception is defined as one of the following:
    a. Barrier method: condoms or occlusive cap with spermicides.
    b. True abstinence: When it is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g. calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.

c. Have had tubal ligation or bilateral oophorectomy (with or without hysterectomy).
d. Male partner sterilisation. The vasectomised male partner should be the only partner for the female participant.
e. Use of established oral, injected or implanted hormonal methods of contraception and intrauterine device

12. Pregnant or lactating women.
13. Males who do not agree to an effective form of contraception for the duration of the study and for 6 months after their last injection for the trial.
14. Hypersensitivity to the active ingredients aflibercept, bevacizumab or ranibizumab or any of the excipients of these drugs.
15. Hypersensitivity to Chinese Hamster Ovary (CHO) cell products or other recombinant human or humanised antibodies
16. A condition that, in the opinion of the investigator, would preclude participation in the study.
17. Participation in an investigational trial involving an investigational medicinal product within 90 days of randomisation.

SAFARI

Long Title:
A Phase IV, prospective, open-label, uncontrolled, European Study in patients with neovascular Age-related macular degeneration (nAMD), evaluating the efficacy and safety of switching from intravitreal Aflibercept to Ranibizumab 0.5mg.

Sponsor:	Novartis
Start Recruitment:	30th June 2016
End Recruitment:	24th March 2015
Duration of Study:	6 months
Number of patients to be recruited:	5

Inclusion Criteria

1. Age ≥50 years.
2. BCVA ≥23 ETDRS letters in study eye
3. Evidence of active CNV involving the center of the fovea in study eye

Patient subgroup specific inclusion criteria
Patients need to meet all the criteria for one of the following two groups:

Group 1. Primary treatment failure

1. Initiated treatment with Aflibercept <130 days prior to the Screening Visit.
2. No increase in BCVA (≥5 letters) since commencing treatment with Aflibercept.
3. Disease activity has never been controlled in the study eye after initiating aflibercept as defined by at least one of the following:evidence of unchanged or increasing retinal* or sub-retinal fluid; new PED; unchanged or increasing size of pre-existing PED.

Group 2. Suboptimal treatment response

1. Aflibercept commenced ≥6 months prior to the Screening Visit.
2. Received ≥3 Aflibercept injections into the study eye within 6 months of the Screening Visit.
3. Evidence of previous reduced disease activity (as defined by reduction of ≥50μm in CSRT on OCT) noted in the study eye after initiating Aflibercept.
4. At Screening Visit, disease activity has worsened (as defined by increasing retinal* or sub retinal fluid, or new or increasing size of PED) in the study eye compared to prior visits.
   *Evidence of increasing retinal fluid may include increased number, size or total volume of IRCs, or increased central retinal or foveal thickness, or similar quantitative retinal imaging data recorded within the individual patient record.

Exclusion Criteria

Exclusion criteria for systemic medical history and conditions

1. History of cerebrovascular accident, transient ischemic attack or myocardial infarction within 3 months of the Screening visit.
2. Uncontrolled blood pressure

Exclusion criteria for ocular medical history and conditions for either eye

1. Evidence of bilateral active CNV during the Screening Period or at Baseline requiring bilateral anti-VEGF injections*.
2. Prior intravitreal injection of Ranibizumab or Bevacizumab into the study eye and/or prior intravitreal injection of Bevacizumab into the fellow eye.
   *Patients with active CNV in the study eye with quiescent CNV in the fellow eye who may have received IVT aflibercept or ranibizumab injections into the fellow eye >40 days prior to Screening, are not excluded from the Study. However, should the fellow eye require anti-VEGF treatment during the study, only ranibizumab may be utilized.

Study eye exclusion criteria

1. Cataract (if causing significant visual impairment), aphakia, severe vitreous hemorrhage, rhegmatogenous retinal detachment, proliferative retinopathy or choroidal neovascularization of any other cause than wet AMD (e.g. ocular histoplasmosis, pathologic myopia (≥-6 dioptres)) at the time of Screening and Baseline.

2. Irreversible structural damage involving the center of the fovea (e.g. advanced fibrosis or geographic atrophy) which in the opinion of the Investigator is sufficient to irreversibly impair visual acuity.
3. Polypoidal choroidal vasculopathy (PCV), RPE tear, central serous retinopathy (CSR), or significant vitreomacular traction identified during Screening period or within 4 months of Baseline visit. Note that small vitreomacular adhesions that do not result in deformity of the retina are permitted.
4. Unable to obtain at Screening OCT images of sufficient quality to be analyzed.

INJECT

Long Title:
Investigation of Jetrea in patients with confirmed Vitreomacular traction.

Sponsor:	Alcon
Start Recruitment:	07th June 2014
End Recruitment:	30th September 2015
Duration of Study:	12 months
Number of patients to be recruited:	7

During this **observational** study patients with VMT will be treated with Ocriplasmin according to NICE guidelines and standard of care. The aim of the study os to evaluate the safety, clinical effectiveness and health related quality of lifeoutcomes in a real-world setting.
No additional examinations or appointments will be required and the study only collects existing data or the data collected in the course of routine treatment of VMT.

CLARITY

Long Title:
Clinical efficacy and mechanisitic evaluation of Aflibercept for Proliferative Diabetic Retinopathy. A multicentre phase IIb randomised active-controlled clinical trial.

Sponsor:	Moorfields Eye Hospital
Start Recruitment:	01st March 2015
End Recruitment:	01st December 2015
Duration of Study:	24 months
Number of patients to be recruited:	12

Inclusion Criteria

1. Subjects of either sex aged 18 years or over.
2. Diagnosis of diabetes mellitus (type 1 or type 2).
3. Best corrected visual acuity in the study eye better than or equal to 54 ETDRS letters (Snellen visual acuity 6/18).
4. PDR with no evidence of previous PRP or presence of new or persistent retinal neovascularisation despite prior PRP that (a) requires treatment in the opinion of the investigator and (b) there is sufficient space in the peripheral retina to performmore PRP treatment. In patients with both eye involvement, the eye with no PRP or the least number of PRP burns will be randomised as the study eye. If both eyes have had no PRP before, the eye with the better visual acuity will be randomised as the study eye.
5. Media clarity, pupillary dilation and subject cooperation sufficient for adequate fundus photographs. Eyes with mild pre-retinal haemorrhage or mild vitreous haemorrhage that does not interfere with clear visualisation of the macula and optic disc are eligible for this study.
6. Ability to give informed consent
7. Women should use effective contraception, be post-menopausal for at least 12 months prior to trial entry, or surgically sterile.

Exclusion Criteria

The following exclusions apply to the study eye only (i.e. they may be present for the non-study eye):
1. Co-existent ocular disease that will affect visual outcome.
2. Moderate or dense vitreous haemorrhage that prevents clear visualisation of the macula and/or optic disc or prevents PRP treatment.
3. Significant fibrovascular proliferation or tractional retinal detachment in the posterior pole.
4. Prior vitrectomy.
5. Presence of macular oedema at baseline confirmed by SD-OCT as central subfield thickness of more than 300µm due to the presence of morphological evidence of diffuse or cystoid oedema. Please see rescreening of patients.
6. Other causes of retinal neovascularisation.
7. Iris or angle neovascularisation and neovascular glaucoma.
8. Anticipated need for cataract extraction or vitrectomy within the next 12months.
9. Known allergy to fluorescein or any components of aflibercept formulation.
10. Previous intravitreal anti-VEGF or steroid treatmentfor diabetic macular oedema in the last 4 months.
11. Panretinal photocoagulation within the last 8 weeks.
12. Aphakia.
13. Uncontrolled glaucoma as per investigator's judgement.
14. Severe external ocular infection.

Exclusion criteria also apply to systemic conditions as follows:
15. The participant should not have an HbA1C level of more than 12%.
16. The participant should not have a blood pressure of more than 170/110 mmHg.
17. A medical condition that, in the opinion of the investigator, would preclude participation in the study.
18. Myocardial infarction, stroke, transient ischaemic attack, acute congestive cardiac failure or any acute coronary event within 6 months of randomisation.
19. Dialysis or renal transplant.
20. Pregnant women.

21. Women of child bearing potential who do not agree to use effective contraception during the study and for at least 3 months after the study has finished.
22. Breast feeding women.
23. Males who do not agree to use an effective form of contraception for the duration of the study and for 3 months after the study has finished.
24. Participation in an investigational trial involving an investigational medicinal product within 30 days of randomisation.

STAR

Long Title:
StereoTactic radiotherapy for wet Age-Related macular degeneration (STAR): A rendomised, double-masked, sham-controlled, clinical trial comparing low-voltage X-Ray irradiation with as needed Ranibizumab, to as needed Ranibizumab monotherapy

Sponsor:	Kings College London and Kings College Hospital
Start Recruitment:	TBC
End Recruitment:	TBC
Duration of Study:	48 months
Number of patients to be recruited:	?15

Inclusion Criteria

1. Participants must have neovascular AMD in the study eye, for which they have received at least 3 prior intravitreal injections of either bevacizumab (Avastin), aflibercept (Eylea), ranibizumab (Lucentis), or pegaptanib (Macugen).
2. Participants must have received an anti-VEGF injection in the study eye within 3 months prior to enrolment.
3. Participants must require treatment with anti-VEGF therapy at the time of enrolment, due to OCT evidence of subretinal fluid and/or cystoid macular oedema, and a macular volume that is greater than the 95th percentile of normal for the SD-OCT machines used in the investigational sites.
4. Participants must be at least 50 years of age.

Exclusion Criteria

1. Disciform scarring that involves the fovea, in the study eye.
2. Geographic atrophy that involves the fovea, or an area of geographic atrophy that is more than 500 microns in greatest diameter, immediately adjacent to the fovea, in the study eye.
3. Visual acuity worse than 6/96 (24 ETDRS letters) in the study eye.
4. Lesion size greater than 4 mm in greatest linear dimension, or greater than 2 mm from the centre of the fovea to the furthest point on the lesion perimeter.
5. Distance from the center of the fovea to the nearest edge of the optic disc less than 3 mm in the study eye (this distance is confirmed by the Oraya SRT device software immediately prior to treatment).
6. An axial length of less than 20 mm, or greater than 26 mm, in the study eye.
7. Contraindication or sensitivity to contact lens application, including recurrent corneal erosions, in the study eye.
8. Type 1 or Type 2 diabetes mellitus.
9. Retinopathy in the study eye.
10. Prior or current therapies in the study eye for age-related macular degeneration, other than anti-VEGF agents, including submacular surgery, subfoveal thermal laser photocoagulation, photodynamic therapy (PDT), or transpupillary thermotherapy (TTT).
11. Presence of an intravitreal device in the study eye.
12. Previous radiation therapy to the study eye, head, or neck with the exception of radio-iodine treatment for hyperthyroidism, epimacular brachytherapy to the non-study eye, or Oraya SRT to the non-study eye.
13. Inadequate pupillary dilation or significant media opacities in the study eye, including cataract, which may interfere with visual acuity testing, the clinical evaluation of the posterior segment, or fundus imaging.
14. Likely to need cataract surgery in the study eye, within two years of enrolment.
15. Study eyes with CNV due to causes other than AMD, including presumed ocular histoplasmosis syndrome (POH), angioid streaks, multifocal choroiditis, choroidal rupture, and pathological myopia (greater than 8 Dioptres spherical equivalent). Participants with retinal angiomatous proliferation (RAP) or idiopathic polypoidal choroidal vasculopathy (IPCV) are not excluded.
16. Known allergy to intravenous fluorescein, ICG or intravitreal ranibizumab.
17. Intraocular surgery or laser-assisted in situ keratomileusis (LASIK) in the study eye within 12 weeks prior to enrolment.
18. Prior pars plana vitrectomy in the study eye.
19. Current participation in another interventional clinical trial, or participation in such a clinical trial within the last six months.
20. Unwilling, unable, or unlikely to return for scheduled follow-up for the duration of the trial.

21. Women who are pregnant at the time of radiotherapy.
22. Participants with an implantable cardioverter defibrillator (ICD) or pacemaker implant (or any implanted device) where the device labelling specifically contraindicates patients undergoing X-ray.
23. Any other condition, which in the judgment of the investigator, would prevent the participant from granting informed consent or completing the study, such as dementia, and mental illness (including generalized anxiety disorder and claustrophobia).

EDNA

Long Title:
Eary detection of neovascular Age-related macular degeneration (nAMD)
Study question – "What is the optimum non-invasive test strategy that will robustly detect nAMD in unaffected fellow eyes during follow-up in secondary care of persons with nAMD in the first affected eye.."

Sponsor:	Queens University Belfast
Chief Investigator	Prof Usha Chakavarthy
Start Recruitment:	TBC
End Recruitment:	TBC
Duration of Study:	36 months
Number of patients to be recruited:	?30-50

Inclusion Criteria

1. Newly diagnosed (within last 3 months) nAMD in one eye and an unaffected second eye (confirmed by FFA)
2. About to commence or recently commenced anti VEGF therapy in the first eye
3. Age 50 -95

Exclusion Criteria

1. Patients with a history of namd in both eyes;
2. Namd in study eye detected at baseline;
3. Presenting visual acuity worse than 73 letters;
4. Retinal pathology in the study eye which can confound subsequent assessments (e.g diabetic retinopathy, macular hole);
5. Not undergoing regular monitoring in standard of care;
6. Patients who cannot give informed consent;
7. Unable to undergo a fundus fluorescein angiography (FFA) test;