Sub-Macular Haemorrhage Clinical Research Grant Guidelines for Applicants

EURETINA and Fight for Sight are seeking suitable proposals for the following clinical research study;

A superiority randomised control trial for the resolution of acute sub-macular haemorrhages in patients with exudative AMD, comparing two treatments:

(a) anti-VEGF (aflibercept OR ranibizumab), gas, subretinal rtPA and vitrectomy

Versus

(b) anti-VEGF (aflibercept OR ranibizumab)

Background

Age-related macular degeneration (AMD) is the commonest cause of severe visual impairment in older adults in the developed world. Fight for Sight has identified AMD as one of our four Strategic Programmes focused on finding ways of stopping sight loss.

Sub-macular haemorrhage (SMH) is caused by damage to the blood vessels and is a severe complication in some cases of exudative AMD. The treatment of SMH with intravitreal anti-VEGF, vitrectomy, subretinal injection of tissue plasminogen activator (rtPA) and gas (collectively “displacement treatment”) displaces the haemorrhage away from the macula and has been described in the literature. Similar displacement results have been reported with gas and tPA injections without vitrectomy, but most surgeons feel more comfortable and in control of complications with added vitrectomy. However, the procedure has a significant risk of complications and carries high health care costs. Recently, publications report that intravitreal anti-VEGF monotherapy may be compatible with resolution of SMH and improvement of visual function. To date, no comprehensive statistically powered randomised control trial (RCT) has shown which treatment option is superior.

This research call seeks proposals for a well-designed clinical research study to conclusively present a clear evidence-base for the alternative treatments.

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2 Van Zeeburg EJT, Van Meurs JC. Literature review of recombinant tissue plasminogen activator used for recent-onset submacular hemorrhage displacement in age-related macular degeneration. Ophthalmologica. 2012
Eligibility

- Applicants must have a tenured post at a recognised university, hospital or research institute within the European Union or Switzerland, Iceland, Norway, Israel, Turkey, Moldova, Faroe Islands, Ukraine, Tunisia, Georgia, Albania, Bosnia & Herzegovina, the former Yugoslav Republic of Macedonia, Montenegro, Serbia and Armenia.
- Applicants, including their key research team members, must have a contract of full-time employment which extends beyond the termination date of the grant.
- Applicants should be able to demonstrate prior experience and expertise in having previously conducted an industry or clinically-led randomised controlled trial or large multi-centre study, and have access to a clinical trials unit within their institution with demonstrable experience in running similar studies.
- The proposal should demonstrate the clinical importance of the research to the European and global population, and be broadly translational with the objective of providing a comprehensive evidence base from which a clinical guideline may be produced in due course.
- The grant is a purely clinical research funding initiative for the conduct of clinical research in human participants meeting relevant inclusion and exclusion criteria. No animal work should be proposed as part of the project.

Contact Us

For any queries relating to your proposal please contact Euretina and Fight for Sight [here](#).

All applications must be submitted via Fight for Sight’s [Grants Management System](#). For any queries regarding the use of the system, please email Fight for Sight at Grants@fightforsight.org.uk.
What to expect in the online application form

All applications must be submitted via Fight for Sight’s Grants Management System. You can save your application at any time and return to it. The ‘Save and Close’ button will take you to the Application Summary page. The Application Summary allows you to view the status of your submission, gain access to your application and generate a PDF of your submission. We advise that you regularly generate PDFs of your submission to inspect the formatting and also to circulate amongst your co-applicants and collaborators for input. Navigating between sections of the application will automatically save your submission.

If you intend to prepare your submission offline, we advise that you paste text into the online form from Notepad or an equivalent program. Microsoft Word may introduce additional characters or cause formatting issues. For any queries regarding the use of the system, please email Fight for Sight at Grants@fightforsight.org.uk.

Applicant Details

Lead applicant details
Your basic information and details of your CV are extracted from your user account. You can update your user account details by clicking on ‘Basic Information’ and selecting ‘Update CV’.

Co-applicant details
The co-applicant(s) are required to approve their association and involvement with the application. They will need to create a user account and complete their CV. To add a co-applicant, search registered users by first name and surname. If the person whom you are adding is not on the system, you can add them by entering their email address. An automated email will be sent to each co-applicant granting them access to the system. Co-applicants are able to view the application at all stages, but cannot edit the application. All changes to the form must be made by the lead applicant. You can view the status of your co-applicants participation on the Application Summary page.

Trial collaborators
Collaborators may help by supplying material, specific expertise, access to patients, and patient samples. Select ‘Yes’ if you do have collaborators and you will be prompted to enter their details and upload a letter of support. Letters of support will automatically be added to the Appendix of the application. Please do not include letters supporting collaboration with industry partners. These will be requested in the Study Design section.

Study team expertise
Describe how the specific expertise of the study team will facilitate successful delivery of the proposed study. Please describe the experience that the lead applicant has in managing large multi-centre clinical trials. Please confirm that team members have good clinical practice (GCP) certification where relevant. (Maximum 500 words)
Research Synopsis
The synopsis allows you to detail some key facts of the trial. It includes the title, proposed start date, duration of the trial, a list of the countries where the trial centres are located, the number of patients to be recruited and the trial design e.g. two-arm randomised control trial.

Background
Need for the study
Within this section applicants are required to provide a literature review and a meta-analysis of previous relevant studies if applicable. Your statement must include the rationale of the research question to be addressed, why the study is needed and details of supporting information, including pre-clinical evidence. Place the study in the context of current clinical knowledge regarding sub-macular haemorrhage. (Maximum 1,500 words)

Clinical impact
Justify how your proposed trial will benefit patients, both in terms of outcome and experience, compared to current clinical practice. (Maximum 250 words)

References
You can provide approximately 20-25 references relevant to the project. Please indicate the first author name and initial(s) et al, title, year, journal, issue and first page number for each reference. Highlight references in bold where you are a co-author. Posters, oral presentations or papers submitted / under review cannot not be used as references. (Maximum 550 words)

Study Design
Trial design
Provide a full description of the clinical trial protocol and study design. Please include details about the study interventions to be used and dosage. Your trial design should include information about pharmacokinetics and pharmacodynamics, duration of treatment and follow up, primary and secondary outcome measures. At a minimum, outcome measures should include ETDRS distance vision at 6 and 12 months, scotoma size, VFQ-25 and safety.

You should define the target patient population for the study and the inclusion and exclusion criteria. Outline of the planned patient assessments including details of baseline collection, visits and assays are required. Please also include justification for each chosen treatment and the rationale for use of an agent(s) with the mechanism of action/target. (Maximum 1,500 words)

Trial scheme
A schematic representation of the trial design is required. You can upload a document that illustrates the scheme of the trial. (Maximum 2 pages)

Detailed statistical analysis plan
Please include information on the randomisation and blinding procedure together with the name and contact details of the statistician who will be responsible for all statistical aspects of the proposed study. Provide a sample size and power calculation with detailed justifications. Also include stratification factors, randomisation ratio, interim analysis, go / no go criteria and safety and
stopping rules (including Adverse Effects, Serious Adverse Effects, and Suspected Unexpected Serious Adverse Reactions). Provide details of how the data will be analysed. **(Maximum 1,000 words)**

**Use of the trial data and dissemination**

Provide details of how the results of the study will be used. For example, will there be a follow on study? What further steps will be required after you have completed your proposed work prior to clinical implementation, or do you anticipate that the results would lead to a change in practice? What publication plan would you propose? **(Maximum 1,000 words)**

**Recruitment plan (table)**

You are required to provide the anticipated recruitment data. Click ‘Add’ to enter the data for each centre. You will be asked to enter the centre, country, the number of patients to be recruited by year and the total number of patients.

<table>
<thead>
<tr>
<th>Centre</th>
<th>Country</th>
<th>Patients Recruited Year 1</th>
<th>Patients Recruited Year 2</th>
<th>Patients Recruited Year 3</th>
<th>Patients Recruited Year 4</th>
<th>Patients Recruited Total</th>
</tr>
</thead>
</table>

A letter of support should be provided by the collaborator and uploaded in the Collaborator section.

**Recruitment curve**

Please upload a figure of the predicted recruitment curve for the trial. **(Maximum 1 side A4)**

**Patient recruitment**

Please address whether you anticipate any challenges in the recruitment of patients and how these will be addressed and overcome if they arise? **(Maximum 200 words)**

**Sourcing of drugs and clinical trial supplies**

State where and how supplies will be provided for the trial (e.g. aflibercept, gas, subretinal rtPA). If any industry collaborations exist in order to obtain items, please upload a letter of support, which will be attached in the Appendix of the application. Please provide all the necessary clinical logistical information required including any qualified person engagement, re-labelling, blinding or other activities required to maintain GCP throughout the duration of the proposed study. **(Maximum 500 words)**

**Trial Management**

**Clinical Trial Unit (CTU)**

You are required to provide details of the primary CTU tasked with the management of the trial. Click ‘Add’ to enter its name, the lead investigator at and location of the CTU.

**Justification of the CTU running the trial**

Please provide justification for the choice of the CTU running the study. You should include details of experience in running RCTs in general and in eye disease specifically. You should also detail the data capture and quality management systems (QMS) that will be in place, and how the unit will lead on
management of the study. Please detail how the proposed study will be
categorised in respect of the relevant EU clinical trial legislation, and in
particular, outline the sponsorship oversight and monitoring activities to be
engaged by the lead applicant. **(Maximum 750 words)**

**Trial Steering Committee**
The study team will need to establish a Trial Steering Committee (TSC) for
governance purposes. The membership should include an independent
chairperson, other independent members, chief investigators and ideally a
public and patient involvement (PPI) representative. Click ‘Add’ to enter the
title, name and institution for each member. Please note that a representative
from EURETINA will be added to the TSC if the grant application is successful.
**Full details of the TSC, including a letter of support, will be required if the
study is funded.**

**Independent Data Monitoring Committee**
The study team will need to establish an Independent Data Monitoring
Committee (IDMC) for data collection strategy. The membership should include
an independent chairperson, and other independent members. Click ‘Add’ to
enter the title, name and institution for each member. **Full details of the IDMC,
including a letter of support, will be required if the study is funded.**

**Ethical approval**
Please describe the proposed clinical trial authorisation procedures and
regulatory outline of GCP and legal obligations for all site jurisdictions. Also
provide a detailed description of the ethical approval processes for all of the
sites involved. **(Maximum 800 words)**

**Patient and Public Involvement (PPI)**
**Lay summary of the proposed study**
Please focus on the purpose of the study, the way(s) in which patients will be
asked to participate and the main potential benefits and risks for patients. This
information will be used for public engagement purposes and should be written
for a non-scientific target audience. **(Maximum 1,000 words)**

**PPI contribution to the study**
Patient and public involvement is a key part of clinical trials. Please describe
how PPI has contributed to the research question, rationale and study design.
Also outline plans for continuing PPI in the governance, management and
delivery of the study. **(Maximum 300 words)**

**Financial Information**
The grant allows for the allocation of up to €2,000,000 between a three to four
year period. All costs should be entered in Pound sterling at an exchange rate
of 0.9 (1 Euro equals 0.9 Pound sterling). Please note that successful grants
will be paid in Euros. The costs should not include any overhead in excess of
2.5% of the value of the study costs. Please note that Fight for Sight is a
registered UK charity exempt from the application of VAT on research charges.

**Total amount requested**
Please enter the total value of the grant. This cannot exceed £1,800,000.
The grant budget is split into three headings;
  o Salary (stating the percentage of full time equivalent)
  o Running Costs (which include consumables, equipment, and regulatory fees etc.)
  o Other Expenses (which includes travel, conferences and publication costs)

Please click on the relevant button and follow the onscreen instructions to enter costs under each heading.

**Justification of costs**
Please provide a brief justification for the budget requested.
(Maximum 300 words)

**Declaration**
Lead applicant must abide by the following statements in order to submit the grant application;
  1. I will be responsible for the day-to-day supervision of the research
  2. My contract in the Host Institution lasts at least as long as the duration of the award
  3. I have read Fight for Sight's Terms and Conditions and agree to abide by them
  4. I confirm that I fully understand the responsibilities of a trial 'sponsor', as per relevant legislation, and that the host institution will act as trial sponsor for this clinical trial

Check boxes will appear on the form. By checking the boxes you confirm agreement to the statements. The declaration needs to be dated once these are all confirmed.

**Authorised Signatories**
In order for your application to be fully submitted for consideration it must be authorised by two signatories. These include the Head of Department of the host institution and a finance representative who has sufficient authority to approve the grant budget requested on behalf of the host institution. The lead applicant must provide the name and details of the signatories. Additionally, the Head of Department must provide a letter of support which should be uploaded through their account in the ‘My Approvals’ section. It is the responsibility of the lead applicant to liaise the Head of Department to ensure that this is completed before the deadline.

Please note that the two signatories must confirm their acceptance of the application for it to be fully submitted for consideration. This must occur before the application deadline date. Please take this additional time into account when completing your application. We advise that you correspond closely with your signatories throughout the submission process.

**Validation Summary**
The Validation Summary highlights any incomplete sections of your submission. Please note that the co-applicants must confirm their participation in order for the submission to be considered complete.
Submitting Your Application

Once your application is complete click ‘Save and Close’. To submit the proposal click on the ‘Submit’ button which will now be active. You will receive an automated email confirming your submission. You will also receive an email once your signatories have completed their responsibilities.

Deadlines

The Deadline for submissions is 5pm GMT (6pm Central European Time) on Wednesday 31 October 2018.

Grants are made on a fully competitive and peer reviewed basis. Fight for Sight is a member of the Association of Medical Research Charities (AMRC) and complies with its guidelines for best practice. EURETINA and Fight for Sight reserve the right to not award any grant funding if none of the submitted applications are deemed to be of sufficient quality. No correspondence will be entered into in relation to grant decisions.

Sponsor responsibilities and clinical trial funding agreement:

- Under no conditions shall EURETINA or Fight for Sight hold any of the responsibilities or obligations of a trial “sponsor” (as defined in any of the relevant legislation or guidelines, including the EU Clinical Trials Directive 2001/20/EC, the pending EU Regulation 536/2014, their equivalent national legislation in any jurisdiction, ICH-GCP, or any other relevant clinical trial guidance).
- Any submission made to this research call shall include a written confirmation from the applicant’s host institution that the applicant, and the duly authorised officer of the host institution, fully understand and acknowledge all of the legal obligations and responsibilities of a trial “sponsor”, as per relevant legislation and guidelines, and that the applicant holds full authority from their institution to make an application to this research call to potentially act as a clinical trial “sponsor”.
- Any successful applicant shall be required to enter into a legally binding clinical trial research funding agreement between the parties prior to the finalisation of a formal grant agreement.