## ORANGE Study: Bleeding on oral anticoagulants (OACs)

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The most common indication for receiving oral anticoagulant therapy is atrial fibrillation (AF). The National Institute for Health & Care Excellence (NICE) estimate that around 2% of the UK population has AF but only about 500k are actually being anticoagulated for it. It is projected that this number is likely to increase to around 1 million AF patients with the new initiatives currently in place, reflecting the efficacy of warfarin and the new oral anticoagulants (NOACs) in stroke prevention.

The second most common indication for anticoagulation is venous thromboembolism (VTE) with an estimated 100k cases per year, followed by mechanical heart valve replacements.

Based on the number of people on oral anticoagulants and a major bleeding rate of around 2% per year, it is estimated there are approximately 20,000 major bleeds per year related to oral anticoagulant use in the UK. Healthcare professionals (HCPs) have long been accustomed to managing warfarin-related bleeds and there was concern surrounding bleeding when the NOACs were introduced since they lacked an antidote. The management of bleeding on oral anticoagulants may vary across the countries that participated in the trials of the NOACs in AF and VTE treatment.

The ORANGE Study, led by Peter MacCallum and Laura Green, has been set up with funding from the British Society for Haematology to look at the outcomes of major bleeding on oral anticoagulants in the UK. It involves a prospective, multicentre, observational 3 year study with data collected on the current management and outcomes of patients who develop major bleeding while on OACs (warfarin, rivaroxaban, dabigatran, apixaban and others as they become available).

### *Primary Objectives*

- Measure the proportion of patients who develop major bleeding and:
    - present with ICH
    - die within 30 days of presentation

### *Secondary Objectives*

- Estimate the effectiveness of products (PCC, rFVIIa or FEIBA, FgC) in treating major bleeding
- Characterise coagulation abnormalities of major bleeding associated with the new OAC
- Examine associations between clinical outcomes and:
    - transfusion requirements (RBC to FFP ratio)
    - correction of coagulation abnormalities resulting from blood transfusion and/or other products

Research Ethics Committee (REC) approval was obtained and the study was National Institute for Health Research, Clinical Research Network (NIHR CRN) Portfolio adopted. Recruitment began in October 2013 with the study due to end in December 2016. There are

31 sites currently recruiting and an interim analysis was presented at the BSH 2015 meeting in Edinburgh.

The presentation to the User Group included an updated interim look at results, however data collection is continuing.

Over 1,000 cases were reported between October 2013 and August 2015. The median age was 79 years and males and females were equally represented.

Approximately 86% of the bleeds were in patients on warfarin and the remainder were on one or other of the NOACs.

Indications for OACs were approximately: 60% AF; 20% VTE; 10% heart valve; 5% stroke; and 5% other.

To date, patients on warfarin had more intracranial bleeding, whilst NOAC patients experienced more gastrointestinal bleeding.

Outcomes at 30 days showed about 60% of patients had been discharged; 20% had died; 13% were still inpatients; and the remainder of the outcome reports were pending.

The study is ongoing for a further year and the results will be presented following that.