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| **Study Title** | Allopurinol and cardiovascular outcomes in patients with ischaemic heart disease (**ALL-HEART**) |
| **NIHR Portfolio Ref** | UKCRN ID 15328; IRAS ID 135900 |
| **Sponsor**  **Funder**  **Principle Investigator** | University of Dundee / NHS Tayside  NIHR HTA  Professor Chris Hawkey – University of Nottingham |
| **Study design** | Interventional: A multi-centre, controlled, prospective randomised open-label blinded endpoint (PROBE) trial. |
| **Study Aim and Objectives (refer to protocol for full details)** | Primary Objective:  To determine whether the addition of allopurinol 600mg daily to usual therapy improves cardiovascular outcomes.  Secondary Objectives:  Cost-effectiveness of adding allopurinol 600mg daily to usual therapy.  Assessment of quality of life  Safety and tolerability |
| **Practice target & study duration** | Practice target: 13 patients; 5215 target overall  Average follow-up of 4 years.  Study is endpoint driven - the study will end when 631 adjudicated primary endpoints have occurred. |
| **Recruitment period** | The study will run from February 2015 to December 2015 |
| **Summary of Eligibility Criteria (refer to protocol for full criteria)** | **Inclusions**   * Male or female patients aged 60 years and over. * Ischaemic heart disease (IHD) defined as a diagnosis of angina or myocardial infarction (MI) at any time or other evidence of ischaemic heart disease (investigator opinion).   **Main exclusions:**  History of gout, known renal impairment (eGFR <60 ml/min),  moderate to severe heart failure (NYHA III-IV), significant hepatic disease, previous allergy to allopurinol, previous serious adverse cutaneous (skin) reaction to any drug, patients already taking urate lowering therapy, patients taking azathioprine, mercaptopurine, ciclosporin or theophylline.  10. Malignancy (except non-metastatic, non-melanoma skin cancers, cervical in-situ carcinoma, breast ductal carcinoma in situ, or stage 1 prostate carcinoma) within the last 5 years (investigator opinion). |
| **Study Activities** | Primary care practice lists will be searched for suitable subjects with IHD who will be invited to participate. At a screening visit, written informed consent will be taken, inclusion and exclusion criteria checked and blood samples taken for baseline full blood count, urea and electrolytes, creatinine, eGFR and urate. Patients will be randomised via a web portal or interactive voice response system (IVRS) to either allopurinol or no drug to be given in addition to their usual medications. Allopurinol will be started at 100mg daily for 2 weeks, then titrated to 300mg daily for 2 weeks, then titrated to 600mg daily if tolerated. Inpatients randomised to allopurinol, bloods will be taken for full blood count, urea and electrolytes, creatinine, eGFR and urate 6 weeks after starting study medication. Patients will be asked to report any treatment-related adverse events, particularly rash (~1% incidence with allopurinol) and gout flares, and any serious adverse events. Study medications will be prescribed by the GP. An eCRF and dedicated study web portal will be used to collect study data and aid pharmacovigilance reporting and trial management. Patients will receive questionnaires annually to complete, which will be posted out by the study sponsor. |
| **Practice Activities** | * GCP-trained GP to act as Site Study Coordinator (SSC) to lead on the study * Practice to search electronic patient records for potentially eligible patients * SSC will review list to confirm eligibility for inviting and screening * Once list checked by GP, arrange for the invitation letters to be mailed to patients using Docmail. * Provision of a room and facilities for research nurse to conduct baseline clinics * Prescribe allopurinol to those randomised to this arm * GP to report any serious adverse events and treatment-related adverse events (via a web-based portal) |
| **Assurances** | Approvals will be obtained for the trial from ethics committees, the Medicines and Healthcare products Regulatory Agency (MHRA) and local research and development departments. Assurance documentation will be provided to the practice who will be asked to return a signed agreement. |
| **Practice reimbursement** | An estimated NHS service support payment of £xxx has been calculated for this study. This figure is based upon the information provided by the study team regarding the likely activities to be performed by your practice; it is an approximation only and may be adjusted in line with the level of practice activity and the amount of CRN support received |
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