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Ibuprofen plus paracetamol in knee pain

Submission date 16/04/2008	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 09/05/2008	**Overall study status** Completed	
Last Edited 18/10/2011	**Condition category** Signs and Symptoms	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
NL0605

Study information

Scientific Title
A randomised, double-blind, parallel group, multiple-dose 3 month study of ibuprofen 400 mg alone, paracetamol (acetaminophen) 1000 mg alone, ibuprofen 200 mg plus paracetamol 500 mg and ibuprofen plus paracetamol 1000 mg, all taken three times daily, in community patients with chronic knee pain

Study objectives
That the efficacy of the combination product is superior to that of either active alone and that the tolerability profiles of all treatments are similar.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Southampton & South West Hampshire Research Ethics Committee A, approved in March 2007 (ref: 07/Q1702/19)

Primary study design
Interventional

Study design
Randomised, double-blind, controlled trial.

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Knee pain

Interventions
Arm 1: Ibuprofen (oral) 400 mg alone
Arm 2: Paracetamol (oral) 1000 mg alone
Arm 3: Ibuprofen (oral) 200 mg plus paracetamol (oral) 500 mg
Arm 4: Ibuprofen (oral) 400 mg plus paracetamol (oral) 1000 mg

All taken three times daily for 3 months.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Ibuprofen and paracetamol.

Primary outcome(s)
1. Safety:
Incidence of moderate and severe adverse events (AEs) classed as possibly, probably or definitely related to treatment. This will be expressed as incidence on a person days basis. AEs will be recorded throughout the study in patient diaries and in the Case Report Form (CRF) in response to questioning by the Investigator at each patient visit (day 10, end week 7, end week 13). Clinically significant changes as judged by the Investigator in haematology, clinical chemistry, urinalysis values or vital signs (including ECGs) will be recorded as adverse events.

2. Short-term efficacy:
The Western Ontario and McMaster Universities osteoarthritis index (WOMAC OA index) subscale for pain (normalised to 0-100 scale) at day 10.

3. Long-term efficacy:
Patient global assessment of study medication after 13 weeks treatment. This will be assessed on a 5 point Likert scale (excellent, good, fair, poor, unacceptable) in response to the question "overall, taking into account both how your medicine worked for you and any side effects you think it caused you, how would you rate your medication as a treatment for your painful knee?" Patients without week 13 assessment data will have their latest recorded value carried forward.

Key secondary outcome(s)
1. Incidence of all adverse events classed as possibly, probably or definitely related to treatment
2. Incidence of all adverse events regardless of relationship to treatment
3. Patient assessment of knee pain using the question "Thinking only of the pain you felt in your knee during the last 48 hours, if you were to remain with that pain for the rest of your life would that be acceptable to you?" (Yes/No) assessed at day 10, end week 7, end week 13 and at endpoint (Last observation carried forward [LOCF])
4. Patient assessment of pain in the signal knee using the WOMAC OA Index sub-scale for pain (normalised to 0-100 scale) at end of week 7, end of week 13 and at endpoint (LOCF)
5. Patient assessment of physical function of the signal knee using the WOMAC OA Index subscale for physical function (normalised to 0-100 scale), at day 10, end of week 7, end of week 13 and at endpoint (LOCF)
6. Patient assessment of joint stiffness in the signal knee, using the WOMAC OA Index subscale (normalised to 0-100 scale) for stiffness at day 10, end of week 7, end of week 13 and at endpoint (LOCF)
7. Composite WOMAC OA index score for the signal knee at day 10, end of week 7, end of week 13 and at endpoint (LOCF)
8. Patient global assessment of study medication at end of day 10 and end of week 7
9. Quality of life (QoL) as assessed by the 36-item Short Form health survey (SF-36) at day 10, end of week 7, end of week 13 and at endpoint (LOCF) (Generic QoL)
10. Quality of life as assessed by the Patient Generated Index questionnaire at day 10, end of week 7, end of week 13 and at endpoint (LOCF). (Patient centred QoL)

Completion date
17/05/2008

Eligibility

Key inclusion criteria
1. Age 40 years and over, both males and females
2. Primary diagnosis of knee pain, as evidenced by the presence of pain in or around at least one knee for most days over the last 3 months and on at least four of the seven days preceding screening visit
3. Pain of the signal knee prior to provision of study medication and where necessary, after an appropriate washout period on discontinuation of any current analgesic medication, at a level of >30mm and <80 mm on the visual analogue scale (VAS) (pain experienced in the previous 24 hours walking on the flat)
4. Be anticipated to require continuous treatment to control pain for the duration of the study

5. Have a Steinbrocker functional capacity classification of 1-3
6. Be registered with a general practitioner
7. Be able to give written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Concomitant other major rheumatic disease (including rheumatoid arthritis, gout and sero-negative arthropathies) or other painful conditions which could interfere with the accurate assessment of the signal knee, or acute joint trauma of the signal knee or a lower limb joint prosthesis
2. An anticipated need for any major surgical procedure or any invasive procedure that would be performed on either knee during the course of the study
3. An active malignancy of any type (subjects who have a history of basal cell carcinoma that has been successfully treated are eligible). Subjects with a history of other malignancies that have been surgically removed and who have no evidence of recurrence for at least five years before study enrolment are also eligible)
4. An active or suspected peptic or duodenal ulceration or gastrointestinal bleeding or severe dyspepsia experienced for most days of the previous month
5. Inflammatory bowel disease (e.g., Crohn's disease or ulcerative colitis), a chronic or acute renal or hepatic disorder, a significant coagulation defect, or any previous history of allergy or known intolerance to any of the drugs or formulation constituents which, in the Investigator's opinion, might preclude use of an non-steroidal anti-inflammatory drug (NSAID), including aspirin sensitive asthma or a previous allergic response to a NSAID, including bronchospasm, urticaria, angioedema and rhinitis
6. Ankle oedema
7. Concomitant medications and treatments: Receipt of any intra-articular hyaluronate in the previous 6 months, or intra-articular corticosteroids within 3 months to the signal joint or intra-articular corticosteroid to any joint within the previous 1 month, or intra-muscular (i.m.) corticosteroid or per oral (p.o.) steroid within the previous month or fluid evacuation without steroid injection, or any drug intended to modify joint structure or function; Subjects taking >325 mg aspirin per day for non-arthritic reasons, if stable for at least 30 days prior to first dose of study medication, are eligible; If the patient uses a cane or other assisted devices at time of initial evaluation, then the usage must remain unchanged. If the patient is undergoing physiotherapy at the time of initial evaluation, then the regimen must remain unchanged throughout the study
8. An anticipated need for treatment with other analgesics (such as opiodis/narcotics) during the course of the study
9. Abnormal pre-treatment laboratory test values >1.5 times the upper limit of normal (ULN) for either aspartate transaminase (AST; SGOT) or alanine transaminase (ALT; SGPT) or any other laboratory abnormalities considered by the Investigator to be clinically significant. If such a value

is found at screening, the patient must be excluded
10. Abuse of alcohol, as evidenced by averaging more than 21 units per week for men or 14 units for women
11. Woman of childbearing potential, who are pregnant or lactating, seeking pregnancy or failing to take adequate contraceptive precautions, (i.e. an oral contraceptive, an approved hormonal implant, an intrauterine device or condoms/diaphragm and spermicide). A woman of childbearing potential is defined as any female who is less than 2 years post-menopausal or has not undergone an hysterectomy or surgical sterilisation, e.g. bilateral tubal ligation, bilateral ovariectomy (oophorectomy). Women of childbearing potential practising sexual abstinence, and those with a partner who has had a vasectomy, who are not using (or are not willing to use) any of these methods of contraception nor undergone the surgical procedures, must be excluded from the study
12. Those previously randomised into the study
13. Those who have participated in a clinical trial in the previous 30 days
14. Those unable in the opinion of the Investigator to comply fully with the study requirements

Date of first enrolment
01/06/2007

Date of final enrolment
17/05/2008

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Division of Academic Rheumatology
Nottingham
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Sponsor information

Organisation
RB Corporate Services Ltd (UK)

ROR
https://ror.org/01g87hr29

Funder(s)

Funder type
Industry

Funder Name
RB Corporate Services Ltd (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2011		Yes	No