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A two part study examining the safety and efficacy of fixed-dose combinations of ibuprofen plus acetaminophen for adults with dental pain following molar extraction

Submission date
08/06/2010

Recruitment status
No longer recruiting

Registration date
24/06/2010

Overall study status
Completed

Last Edited
20/02/2020

Condition category
Oral Health

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

NL0604

Study information

Scientific Title
A two part study examining the analgesic efficacy and tolerability of three fixed-dose combinations of ibuprofen plus acetaminophen for adults with dental pain following third molar extraction: A double-blind, parallel-group, placebo-controlled, randomised, repeat dose trial with two-centre factorial design

Study objectives
This was a two-part study. The objective of Part 1 was to assess the efficacy and tolerability of a fixed-dose combination tablet containing ibuprofen and acetaminophen (paracetamol) (ibuprofen 100mg plus acetaminophen 250 mg, ibuprofen 200 mg plus acetaminophen 500 mg, and ibuprofen 400 mg plus acetaminophen 1000 mg) and compare with placebo, ibuprofen 200 mg, ibuprofen 400 mg, acetaminophen 500 mg, and acetaminophen 1000mg in terms of total analgesic effect, peak analgesic effect onset and duration of action, and the subjects overall assessment of the study medication.

The objective of Part 2 was to assess the efficacy and tolerability of a fixed-dose combination tablet containing ibuprofen and acetaminophen (ibuprofen 100 mg plus acetaminophen 250 mg ibuprofen 200 mg plus acetaminophen 500 mg, and ibuprofen 400 mg plus acetaminophen 1000 mg) and compare with each other and placebo in terms of analgesic effect and the subjects overall assessment of the study medication.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Coast Independent Review Board approved on the 5th June 2007

Study design
Multicentre double blind randomised placebo controlled parallel group single and multiple dose phase factorial design two-part study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details below to request a patient information sheet

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

Interventions
This was a two part study, the objective of Part 1 was to assess the efficacy and tolerability of a fixed-dose combination tablet containing ibuprofen and acetaminophen as follow:
1. Ibuprofen 100mg plus acetaminophen 250mg
2. Ibuprofen 200mg plus acetaminophen 500mg
3. Ibuprofen 400mg plus acetaminophen 1000mg
and compared with :
1. Placebo
2. Ibuprofen 200mg
3. Ibuprofen 400mg
4. Acetaminophen 500mg and
5. Acetaminophen 1000mg

In terms of total analgesic effect, peak analgesic effect, onset and duration of action and the subjects overall assessment od the study medication.

The objective of Part 2 was to assess the efficacy and tolerability of a fixed-dose combination tablet containing ibuprofen and acetaminophen as follows:
1. Ibuprofen 100mg plus acetaminophen 250mg
2. Ibuprofen 200mg plus acetaminophen 500mg and
3. Ibuprofen 400mg plus acetaminophen 1000mg
and compare with each other and placebo in terms of analgesic effect and the subjects overall assessment of the study medication.

Subjects were randomly allocated to one of the eight treatment groups.

All subjects remained at the study centre and were monitored for approximately 80 hours after the first dose of study medication (8 hours in Part 1 and 72 hours in Part 2) and returned for a post-operative visit seven to ten days after surgery. Each individual subjects participation in the study could have lasted for up to 43 days.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
The primary endpoint in Part 1 was SPRID0-8h and in Part 2 was the number of complete 24-hours periods (as 0, 1, 2, 3) with no more than one dose of rescue medication and with the subjects overall assessment always rated as at least good (i.e., 3, 4, 5)

Secondary outcome measures
1. The key secondary endpoint for Part 1:
1.2. The first recorded post-baseline assessment of the subjects overall assessment of the study medication as a treatment for pain on a 5-point Overall Assessment Categorical Rating Scale. This variable was assessed at 8 hours or just prior to administration of rescue medication if sooner

1.3. Duration of pain half gone. This was calculated in a analogous was to TOTPAR but using zero (pain not half gone) and one (pain half gone)
1.4. Time to meaningful PAR using the two-stopwatch technique
1.5. Duration of the effect measured as time to first administrate of rescue medication. Rescues medication taken after withdrawal was disregarded for analysis purposes

2. The key secondary endpoint part 2:
2.1. The time of treatment failure was taken as the time of withdrawal or the timing of the inadmissible dose of study/rescue medication, whichever was earlier
2.2. Median score for subjects overall assessment per 24-hours period
2.3. Mean number of dose taken per 24-hours (including rescue)
2.4. Mean duration between doses per 24-hour period and overall (including rescue)
2.5. Peak PAR score per 24-hour period

Overall study start date
16/10/2006

Completion date
10/09/2007

Eligibility

Key inclusion criteria
1. Age: Subjects at least 16 years of age were eligible to participate
2. Sex: Both males and females were eligible for entry
3. Primary Diagnosis: At least three impacted third molars (two of which must have been mandibular impacted molars) indicated for removal. Both mandibular impactions must have required bone removal, and there must have been a total score of 9 or greater on the impaction grading scale for the three or four impacted third molar
4. Baseline pain intensity (PI): Subjects must have been experiencing moderate to severe postoperative pain based on the Pain Intensity Categorical Rating Scale and have a PI Visual Analogue Scale (VAS) score of 50mm or greater on the 100mm within 6 hours of completion of surgery, but more than 3 hours after the last administration of fentanyl
5. Subjects who gave written informed consent. Subjects who were 16 or 17 years of age also required their parents or legal guardian to provide written informed consent in addition to their written assent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
A total of 1303 subjects were screened for study enrolment of which 735 were randomised to receive study treatment.

Total final enrolment

735

Key exclusion criteria
1. Those who had participated in a clinical trial in the previous 12 weeks. Twelve weeks calculated from the time of last dosing in the prior trial to time of anticipated first dosing in this trial.
2. A current history of significant disease deemed by the Investigator to render the subject unsuitable for inclusion
3. An ongoing painful condition other than that associated with the current third molar surgery
4. Any ongoing condition that may have interfered with the absorption, distribution, metabolism or excretion of the study medication
5. A history of allergy or intolerance (including angioedema, urticaria, bronchospasm and rhinitis) related to the treatment with ibuprofen, acetaminophen, aspirin, other NSAIDs or any other medication used in this study, including anaesthetics and antibiotics that may have been required on the day of the surgery (Day 1) or the formulation constituents of the study medications
6. A history of frequent peptic ulcers, duodenal ulcers or gastrointestinal (GI) bleeding
7. A history of frequent dyspepsia, heartburn or indigestion
8. A history of migraine headaches within the past year
9. A history of psychotic illness, attempted suicide or neurosis
10. Those unable to refrain from smoking during their stay in the research centre
11. A positive history of drug or alcohol abuse within the past six months
12. Those who were taking any concomitant medication that might have confounded assessments of pain relief (PAR), such as: psychotropic drugs, antidepressants, sedative-hypnotics (other than those permitted for conscious sedation), or other analgesics taken within five times of their elimination half lives. Selective serotonin reuptake inhibitors (SSRIs) and serotonin noradrenalin reuptake inhibitors (SNRIs) were permitted if the subject had been on a stable dose for at least four weeks prior to visit 1 (screening).
13. Those previously randomised into this study
14. Subjects who had received ant analgesic, anti-inflammatory drug, sedative-hypnotic, or caffeine containing food or drink from midnight the night prior to surgery and during the entire 80 hours post-dose assessment period, except for the study medication, perioperative sedative, antibiotics or permitted anaesthetics. The following anaesthetics were permitted lidocaine with epinephrine, nitrous oxide, diazepam (Valium), methohexitol (Brevital) and fentanyl. The following antibiotics were permitted: penicillin, macrolide antibiotics, clindamycin and topical tetracycline gelfoam.
15. Those who were unable, in the opinion of the investigator, to comply fully with the study requirements.
16. Those with abnormal liver function tests at screening
17. A history of epileptic seizures

Date of first enrolment
16/10/2006

Date of final enrolment
10/09/2007

Locations

Countries of recruitment
United States of America

Study participating centre
SCIREX Research Center/ Premier Research Group
Austin
United States of America
TX 78705

Sponsor information

Organisation
Reckitt Benckiser Healthcare (UK)

Sponsor details
Dansom Lane
Hull
United Kingdom
HU8 7DS

Sponsor type
Industry

ROR
https://ror.org/01g87hr29

Funder(s)

Funder type
Industry

Funder Name
Reckitt Benckiser Healthcare (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	01/06/2010	20/02/2020	Yes	No