



Clinical trial results: Paracetamol Treatment in Hypertension: effect on Blood Pressure Study.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2013-003204-40 |
| Trial protocol | GB |
| Global end of trial date | 01 February 2022 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 05 October 2023 |
| First version publication date | 05 October 2023 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | PATHBP_2013 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01997112 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | ACCORD (University of Edinburgh and NHS Lothian) |
| Sponsor organisation address | 47 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ |
| Public contact | Prof David Webb, University of Edinburgh, +44 01312429216, D.J.Webb@ed.ac.uk |
| Scientific contact | Prof David Webb, University of Edinburgh, +44 01312429216, D.J.Webb@ed.ac.uk |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 01 February 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 February 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 February 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of paracetamol on blood pressure in hypertensives adults taking or not taking antihypertensive medications.

Protection of trial subjects:

The trial was conducted in accordance with all relevant data protection, ethical and regulatory requirements to ensure the privacy and security of patient information and to ensure the rights, safety and well-being of the patients and the quality of the research data.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 13 January 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United Kingdom: 110 |
| Worldwide total number of subjects | 110 |
| EEA total number of subjects | 110 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 66 |
| From 65 to 84 years | 44 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Between September 2014 and June 2019 204 patients were identified through: the hypertension service in Edinburgh; NHS Lothian GP Practices; GP ABPM service; SHARE (NHS Research Scotland initiative - to search for willing participants in the SE Scotland). 110 of these were randomised into the trial.

Pre-assignment

Screening details:

Participant's medical history & medication use will be reviewed. Complete physical examination: height, weight, vital signs. Blood taken for full blood count, paracetamol level, coagulation screen, INR, liver, renal function. Participants asked to wear a 24-hour ambulatory blood pressure monitor, if ABPM has not been performed in previous 3 months.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Baseline (overall trial) (Studies 1 + 2) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Paracetamol |

Arm description:

Paracetamol 1g (500mg x2) four times daily, given for 14 days, with a 14-day washout period. (Cross-over trial.)

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Paracetamol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

1g (500mg x 2) four times daily.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Placebo: hard gelatin capsules containing Maize Starch Ph. Eur.

| | |
|--|---------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Two capsules, four times per day. There is a washout phase of 14(+7) days between treatment phases.

| Number of subjects in period 1 | Paracetamol | Placebo |
|--------------------------------|-------------|---------|
| Started | 55 | 55 |
| Completed | 53 | 50 |
| Not completed | 2 | 5 |
| Consent withdrawn by subject | 2 | - |
| Physician decision | - | 5 |

Period 2

| | |
|------------------------------|----------------------------|
| Period 2 title | Sub-study: biomarker study |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|--|----------------------------|
| Arm title | Sub-study: biomarker study |
| Arm description: All participants will be asked to participate in this sub-study. One extra blood sample will be taken at each study visit (10mls) for liver function tests and biomarker analyses. In addition, a blood sample (5mls) will be taken on day 1 for DNA analysis. | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 2 | Sub-study: biomarker study |
|--------------------------------|-------------------------------|
| Started | 103 |
| Completed | 103 |

Period 3

| | |
|------------------------------|---|
| Period 3 title | Sub-study: urinary prostaglandins study |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|--|---|
| Arm title | Sub-study: urinary prostaglandins study |
| Arm description: All females taking part in the baseline studies 1 and 2 will be asked to provide a 24-hour urine collection for PGE and 6-keto-PGF α estimation. A 24-hour urine collection will be performed on four occasions throughout the study, at the start and end of each study drug period. | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| | |
|---|---|
| Number of subjects in period 3^[1] | Sub-study: urinary prostaglandins study |
| Started | 17 |
| Completed | 17 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Of the 17 subjects actually enrolled into the sub-study - 17 started this sub-study and 17 completed the sub-study

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Baseline (overall trial) (Studies 1 + 2) |
|-----------------------|--|

Reporting group description: -

| Reporting group values | Baseline (overall trial) (Studies 1 + 2) | Total | |
|------------------------|--|-------|--|
| Number of subjects | 110 | 110 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 66 | 66 | |
| From 65-84 years | 44 | 44 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 26 | 26 | |
| Male | 84 | 84 | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Paracetamol |
| Reporting group description: Paracetamol 1g (500mg x2) four times daily, given for 14 days, with a 14-day washout period. (Cross-over trial.) | |
| Reporting group title | Placebo |
| Reporting group description: Placebo: hard gelatin capsules containing Maize Starch Ph. Eur. | |
| Reporting group title | Sub-study: biomarker study |
| Reporting group description: All participants will be asked to participate in this sub-study. One extra blood sample will be taken at each study visit (10mls) for liver function tests and biomarker analyses. In addition, a blood sample (5mls) will be taken on day 1 for DNA analysis. | |
| Reporting group title | Sub-study: urinary prostaglandins study |
| Reporting group description: All females taking part in the baseline studies 1 and 2 will be asked to provide a 24-hour urine collection for PGE and 6-keto-PGF α estimation. A 24-hour urine collection will be performed on four occasions throughout the study, at the start and end of each study drug period. | |

Primary: Difference in mean daytime systolic ambulatory BP

| | |
|--|--|
| End point title | Difference in mean daytime systolic ambulatory BP ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: Study: day 1 (visit -1), day 5 (visit 4), day 8 (visit 7) and day 15 (visit 14). Cross-over: day 29 (visit -1), day 33 (visit 4), day 36 (visit 7) and day 43 (visit 14). | |
| Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Arithmetic mean Precision/Dispersion Type: Standard deviation Difference in least square mean: 4.7 Confidence interval: 2.9-6.6 | |

| End point values | Paracetamol | Placebo | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 53 | 50 | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | 4.7 (\pm 2.9) | 4.7 (\pm 2.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in clinic systolic BP

| | |
|---|----------------------------------|
| End point title | Difference in clinic systolic BP |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Study: day 1 (visit -1), day 5 (visit 4), day 8 (visit 7) and day 15 (visit 14). Cross-over: day 29 (visit -1), day 33 (visit 4), day 36 (visit 7) and day 43 (visit 14). | |

| End point values | Paracetamol | Placebo | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 55 | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | 4.6 (\pm 6.7) | 4.6 (\pm 6.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in daytime diastolic ambulatory BP

| | |
|---|---|
| End point title | Difference in daytime diastolic ambulatory BP |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Study: day 1 (visit -1), day 5 (visit 4), day 8 (visit 7) and day 15 (visit 14). Cross-over: day 29 (visit -1), day 33 (visit 4), day 36 (visit 7) and day 43 (visit 14). | |

| End point values | Paracetamol | Placebo | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 55 | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | 1.6 (\pm 2.7) | 1.6 (\pm 2.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in mean daytime systolic ambulatory BP in patients taking and not taking antihypertensive medications

| | |
|-----------------|--|
| End point title | Difference in mean daytime systolic ambulatory BP in patients taking and not taking antihypertensive medications |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Study: day 1 (visit -1), day 5 (visit 4), day 8 (visit 7) and day 15 (visit 14). Cross-over: day 29 (visit -1), day 33 (visit 4), day 36 (visit 7) and day 43 (visit 14).

| End point values | Paracetamol | Placebo | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 55 | | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | 3.6 (\pm 11.3) | 3.6 (\pm 11.3) | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Difference in urinary prostaglandins

| | |
|-----------------|--------------------------------------|
| End point title | Difference in urinary prostaglandins |
|-----------------|--------------------------------------|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Study: start 24hr urine collection (UC) study day 1, finish study day 2; start 24hr UC study day 15, finish study day 16. Crossover: start 24hr UC study day 29, finish study day 2; start 24hr UC study day 43, study day 44.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Difference in liver biomarkers

| | |
|-----------------|--------------------------------|
| End point title | Difference in liver biomarkers |
|-----------------|--------------------------------|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Study: day 1 (visit -1), day 5 (visit 4), day 8 (visit 7) and day 15 (visit 14). Cross-over: day 29 (visit -1), day 33 (visit 4), day 36 (visit 7) and day 43 (visit 14).

| | | | | |
|--------------------------------------|----------------------------------|--|--|--|
| End point values | Sub-study: biomarker study | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[2] | | | |
| Units: U/L | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[2] - Not analysed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Investigators must report all SAEs to the Sponsor within 24 hours of becoming aware of event.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Baseline (overall trial) (Studies 1 + 2) |
|-----------------------|--|

Reporting group description: -

| Serious adverse events | Baseline (overall trial) (Studies 1 + 2) | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 110 (1.82%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Baseline (overall trial) (Studies 1 + 2) | | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 66 / 110 (60.00%) | | |
| Injury, poisoning and procedural complications | | | |
| Accidental injury to right thumb, requiring sutures. | | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Broken tooth. | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Bruised ribs (left sided) post accidental injury. | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Bruised ribs - sporting accident | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Left knee injury | Additional description: Left knee injury- attending Osteopath regularly | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Minor knee injury | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Pulled muscle (strain) right side below rib | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Left leg muscle tear | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Patchy facial flushing | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Atrial Flutter | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| fluttering in his upper left chest | Additional description: Patient noted both yesterday x 3 episodes and today x 4 episodes over a six hour period - fluttering in his upper left chest. No other | | |

| | | | |
|---|--|--|--|
| | symptoms to note. Arrhythmia PMH 2011. Manual pulse taken - regular, strong and around 60 BPM. ECG performed today | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Dizziness/lightheaded | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Headaches | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Occasional headaches | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Right sided sciatica | | | |
| subjects affected / exposed | 2 / 110 (1.82%) | | |
| occurrences (all) | 2 | | |
| Sporadic nerve pain in left forefinger (distal joint). Possible gym injury. | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| light headed | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| poor quality sleep | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| sciatic pain | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Left sided sciatica | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|--|--|
| Lump at left lymph removal site. subjects affected / exposed occurrences (all) | Additional description: Lump at left lymph removal site. Assessed. NAD. | | |
| | 1 / 110 (0.91%) 1 | | |
| Tiredness subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Immune system disorders Hayfever symptoms subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Mild hayfever symptoms of sneezing subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Seasonal hayfever. subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Eye disorders Dry eyes subjects affected / exposed occurrences (all) | 2 / 110 (1.82%) 2 | | |
| Red and Itchy eyes subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Gastrointestinal disorders Gastric upset. Diarrhoea + vomiting x single episode subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Heartburn subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Indigestion subjects affected / exposed occurrences (all) | 4 / 110 (3.64%) 4 | | |
| Mild Nausea subjects affected / exposed occurrences (all) | 3 / 110 (2.73%) 3 | | |

| | | | |
|--|--------------------------------------|--|--|
| Mild stomach ache on occasions subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Mouth ulcers subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Sporadic toothache subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| tooth pain following extraction and abscess subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Gastric upset. subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Nauseous when taking IMP subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Constipation subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Increased bowel movement to twice daily. subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Nausea and vomiting subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Nausea subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Chesty wheeze subjects affected / exposed occurrences (all) Nasal congestion | 1 / 110 (0.91%) 1 | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Patient aware of clearing throat more often. | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Sore throat | | | |
| subjects affected / exposed | 2 / 110 (1.82%) | | |
| occurrences (all) | 2 | | |
| Tickly cough | | | |
| subjects affected / exposed | 2 / 110 (1.82%) | | |
| occurrences (all) | 2 | | |
| Throat pain | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| exacerbation of asthma | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Left forearm lesion | Additional description: Left forearm lesion under review - GP referral to dermatology 21/01/2019 Discharged from appointment with no follow-up except pre arranged 6 monthly visits for monitoring re PMH. | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Night sweats | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Rash over right forearm | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| dry skin on legs and armpits | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Cellulitis/Allergic reaction/Photosensitivity | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Itching round ankles | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Rash on right forearm | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Itchy rash on forehead & neck | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Backache | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Lower back ache | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Painful left ankle | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Right Achilles tendon pain | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Right sided ache under ribs | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| right knee pain | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Lower back pain | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Slight swelling both ankles | | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Stiffness left shoulder and neck. | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| left knee pain | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Right ankle Achilles tendon tenderness | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Cold symptoms | | | |
| subjects affected / exposed | 9 / 110 (8.18%) | | |
| occurrences (all) | 9 | | |
| Cold symptoms - upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 110 (1.82%) | | |
| occurrences (all) | 2 | | |
| Gum infection followed by a tooth extraction | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Mild infection of left eye. | Additional description: Mild infection of left eye. Over the counter eye drops used and symptoms improving. | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Right eye conjunctivitis | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Sore throat and cold symptoms | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| Viral illness. | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| upper respiratory tract infection | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |
| flu like symptoms | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported