# Clinical trial results:
# Bone Evaluation in HIV-positive women over 40 who Switch from TDF + 3TC/FTC + NNRTI to Triumeq

## Summary

| | |
|---|---|
| EudraCT number | 2015-005297-37 |
| Trial protocol | GB |
| Global end of trial date | 14 February 2020 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 13 December 2021 |
| First version publication date | 13 December 2021 |
| Summary attachment (see zip file) | Clinical Study report (BESTT Clinical Study Report_v3.0_22.11.2021.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 3552 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | King's College Hospital NHS Foundation Trust |
| Sponsor organisation address | Denmark Hill, London, United Kingdom, SE5 9RS |
| Public contact | Dr Frank Post, King's College Hospital NHS Foundation Trust, 0044 20784857795776, frank.post@kcl.ac.uk |
| Scientific contact | Dr Frank Post, King's College Hospital NHS Foundation Trust, 0044 20784857795776, frank.post@kcl.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 | 28 October 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 February 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 February 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to compare the changes in bone mineral density (BMD) over 96 weeks in women who switch from Truvada/NNRTI to Triumeq, as compared to women who stay on their current Truvada/NNRTI regimen.

Protection of trial subjects:

Patients are free to withdraw consent for study treatment and/or consent to participate in the study at any time and without the prejudice to further treatment. Patients who withdraw from study treatment, but are willing to continue to participate in the follow-up visits, should be followed according to the procedures outlined in the protocol.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 05 May 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United Kingdom: 91 |
| Worldwide total number of subjects | 91 |
| EEA total number of subjects | 91 |

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) | 87 |
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

HIV positive women ≥40 years on stable antiretroviral therapy consisting of TDF/ FTC (or 3TC) plus an NNRTI with HIV RNA <50 copies/mL for at least 12 months will be eligible to enter the trial.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 102[1] |
| Number of subjects completed | 91 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | screen fail: 11 |

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The pre-assignment period includes participants who were screened and then not enrolled into the study

### Period 1

| | |
|---|---|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Switch ABC/3TC/DTG |

Arm description:

Switch to Triumeq (abacavir 600 mg, lamivudine 300 mg, dolutegravir 50 mg), one tablet daily

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Triumeq |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: 600mg abacavir, 300mg lamivudine, 50mg dolutegravir
Daily dose: 1 tablet
Duration of use: 96 weeks

| | |
|---|---|
| **Arm title** | Ongoing TDF/FTC/NNRTI |

Arm description:

Participants who are randomised to arm 2 will continue on their current antiretroviral therapy. This will contain tenofovir disoproxil fumarate, emtricitabine or lamivudine, and an NNRTI (nevirapine, efavirenz, etravirine, rilpivirine), administered singularly or as a fixed dose combination. Fixed dose combinations include Atripla, Eviplera or Truvada plus an NNRTI.

| | |
|---|---|
| Arm type | Active comparator |

| | |
|---|---|
| Investigational medicinal product name | Tenofovir disoproxil fumarate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: 245mg tenofovir disoproxil fumarate
Daily dose: 1 tablet once daily
Duration of use: 96 weeks

| | |
|---|---|
| Investigational medicinal product name | Lamivudine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: 150mg lamivudine or 300mg lamivudine
Daily dose: 300mg daily
Duration of use: 96 weeks

| | |
|---|---|
| Investigational medicinal product name | Truvada |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: 245mg tenofovir disoproxil fumarate, 200mg emtricitabine
Daily dose: 1 tablet
Duration of use: 96 weeks

| | |
|---|---|
| Investigational medicinal product name | Atripla |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: Efavirenz 600mg, emtricitabine 200mg, tenofovir disoproxil fumarate 245mg
Daily dose: 1 tablet
Duration of use: 96 weeks

| | |
|---|---|
| Investigational medicinal product name | Eviplera |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: Rilpivirine 25mg, emtricitabine 200mg, tenofovir disoproxil fumarate 245mg
Daily dose: 1 tablet
Duration of use: 96 weeks

| | |
|---|---|
| Investigational medicinal product name | Efavirenz |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: Efavirenz 600mg tablet or 200mg capsule
Daily dose: 600mg
Duration of use: 96 weeks

| Investigational medicinal product name | Nevirapine |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: Nevirapine 400mg prolonged release (PR) or 200mg tablet
Daily dose: 400mg
Duration of use: 96 weeks

| Investigational medicinal product name | Etravirine |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: 200mg
Daily dose: Etravirine 400mg
Duration of use: 96 weeks

| Investigational medicinal product name | Rilpivirine |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Unit strength: Rilpivirine 25mg
Daily dose: 25mg
Duration of use: 96 weeks

| **Number of subjects in period 1** | Switch ABC/3TC/DTG | Ongoing TDF/FTC/NNRTI |
|---|---|---|
| Started | 59 | 32 |
| Completed | 59 | 32 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Switch ABC/3TC/DTG |
| Reporting group description: | |
| Switch to Triumeq (abacavir 600 mg, lamivudine 300 mg, dolutegravir 50 mg), one tablet daily | |
| Reporting group title | Ongoing TDF/FTC/NNRTI |
| Reporting group description: | |
| Participants who are randomised to arm 2 will continue on their current antiretroviral therapy. This will contain tenofovir disoproxil fumarate, emtricitabine or lamivudine, and an NNRTI (nevirapine, efavirenz, etravirine, rilpivirine), administered singularly or as a fixed dose combination. Fixed dose combinations include Atripla, Eviplera or Truvada plus an NNRTI. | |

| Reporting group values | Switch ABC/3TC/DTG | Ongoing TDF/FTC/NNRTI | Total |
|---|---|---|---|
| Number of subjects | 59 | 32 | 91 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 50.9 | 49.5 | |
| standard deviation | ± 7.0 | ± 6.0 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 59 | 32 | 91 |
| Male | 0 | 0 | 0 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Switch ABC/3TC/DTG |
| Reporting group description: | |
| Switch to Triumeq (abacavir 600 mg, lamivudine 300 mg, dolutegravir 50 mg), one tablet daily | |
| Reporting group title | Ongoing TDF/FTC/NNRTI |
| Reporting group description: | |
| Participants who are randomised to arm 2 will continue on their current antiretroviral therapy. This will contain tenofovir disoproxil fumarate, emtricitabine or lamivudine, and an NNRTI (nevirapine, efavirenz, etravirine, rilpivirine), administered singularly or as a fixed dose combination. Fixed dose combinations include Atripla, Eviplera or Truvada plus an NNRTI. | |

### Primary: • Between study-arm changes from baseline in total hip bone mineral density (BMD) at week 48

| | |
|---|---|
| End point title | • Between study-arm changes from baseline in total hip bone mineral density (BMD) at week 48 |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| baseline to week 96 | |

| End point values | Switch ABC/3TC/DTG | Ongoing TDF/FTC/NNRTI | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 59 | 32 | | |
| Units: g/cm2 | | | | |
| median (full range (min-max)) | | | | |
| Baseline | 0.96 (0.92 to 0.99) | 1.03 (0.98 to 1.08) | | |
| Week 96 | 0.96 (0.93 to 1.00) | 1.02 (0.98 to 1.07) | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Adjusted mean difference between study arms |
| Statistical analysis description: | |
| Intention to treat analyses. | |
| Comparison groups | Switch ABC/3TC/DTG v Ongoing TDF/FTC/NNRTI |

| | |
|---|---|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| P-value | = 0.438 |
| Method | Regression, Linear |

Notes:

[1] - Intention to treat

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: baseline to week 96 | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23 |

| Reporting groups | |
|---|---|
| Reporting group title | Switch ABC/3TC/DTG |
| Reporting group description: Switch to Triumeq (abacavir 600 mg, lamivudine 300 mg, dolutegravir 50 mg), one tablet daily | |
| Reporting group title | Ongoing TDF/FTC/NNRTI |
| Reporting group description: Participants who are randomised to arm 2 will continue on their current antiretroviral therapy. This will contain tenofovir disoproxil fumarate, emtricitabine or lamivudine, and an NNRTI (nevirapine, efavirenz, etravirine, rilpivirine), administered singularly or as a fixed dose combination. Fixed dose combinations include Atripla, Eviplera or Truvada plus an NNRTI. | |

| Serious adverse events | Switch ABC/3TC/DTG | Ongoing TDF/FTC/NNRTI | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 59 (15.25%) | 2 / 32 (6.25%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Hysterectomy | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| perianal abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Attempted suicide | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| papillary carcinoma | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroidectomy | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Mixed connective tissue disease | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| **Non-serious adverse events** | Switch ABC/3TC/DTG | Ongoing TDF/FTC/NNRTI | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 52 / 59 (88.14%) | 25 / 32 (78.13%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| General disorders and administration site conditions | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Abnormal dreams | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 0 / 32 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 0 / 32 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Parasomnia | | | |
| subjects affected / exposed | 4 / 59 (6.78%) | 0 / 32 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Immune system disorders | | | |
| allergic reaction | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 2 | |
| Anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| folic acid deficiency | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| hayfever | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 0 / 32 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| low b12 and folate | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 4 / 59 (6.78%) | 1 / 32 (3.13%) | |
| occurrences (all) | 5 | 1 | |
| Reproductive system and breast disorders | | | |
| Adnexal mass | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| bulky uterus | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Endometrial thickening | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| fibroids | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| menorrhagia | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Postmenopausal bleeding | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| vaginal bleeding | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| vaginal candidasis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 32 (3.13%) | |
| occurrences (all) | 1 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| chest infection | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 2 / 32 (6.25%) | |
| occurrences (all) | 3 | 2 | |
| cold/coryzal symptoms | | | |
| subjects affected / exposed | 5 / 59 (8.47%) | 6 / 32 (18.75%) | |
| occurrences (all) | 5 | 6 | |
| Cough | | | |
| subjects affected / exposed | 9 / 59 (15.25%) | 2 / 32 (6.25%) | |
| occurrences (all) | 10 | 2 | |
| post nasal drip | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Throat irritation | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 1 / 32 (3.13%) | |
| occurrences (all) | 3 | 1 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Depression | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 59 (0.00%) | 2 / 32 (6.25%) | |
| occurrences (all) | 0 | 2 | |
| suicidal thoughts | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| low mood | | | |
| subjects affected / exposed | 4 / 59 (6.78%) | 3 / 32 (9.38%) | |
| occurrences (all) | 4 | 3 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 5 / 59 (8.47%) | 3 / 32 (9.38%) | |
| occurrences (all) | 5 | 3 | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 59 (8.47%) | 2 / 32 (6.25%) | |
| occurrences (all) | 5 | 2 | |
| Headache | | | |
| subjects affected / exposed | 4 / 59 (6.78%) | 2 / 32 (6.25%) | |
| occurrences (all) | 4 | 2 | |
| Migraine | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| neurocognitive symptoms | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Memory impairment | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| itchy eyes | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| bilateral red eyelids | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| sty | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| root canal | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 32 (3.13%) | |
| occurrences (all) | 1 | 1 | |
| Tooth erosion | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| abdominal heat | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Constipation | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |

| | | | |
|---|---|---|---|
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 59 (8.47%) | 2 / 32 (6.25%) | |
| occurrences (all) | 6 | 3 | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Flatulence | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 14 / 32 (43.75%) | |
| occurrences (all) | 1 | 1 | |
| reflux | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| stomach pain | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 0 / 32 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| localised rash | | | |
| subjects affected / exposed | 4 / 59 (6.78%) | 1 / 32 (3.13%) | |
| occurrences (all) | 4 | 1 | |
| athletes foot | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| coldsores | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| darkened patches | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eczema | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Skin infection | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Swollen finger | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Fungal skin infection | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| haemarrhoids | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hot flush | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 32 (3.13%) | |
| occurrences (all) | 1 | 1 | |
| infected hair follicle | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Wound infection | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| itchiness | | | |
| subjects affected / exposed | 4 / 59 (6.78%) | 0 / 32 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Lichen planus | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lipodystrophy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| shoulder lump | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dry skin | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| solar keratosis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 2 / 32 (6.25%) | |
| occurrences (all) | 2 | 2 | |
| Micturition difficulty | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Weight increased | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 0 / 32 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| body pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| painful ankles | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| arm pain | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Back pain | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| lower back muscle spasm | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 15 / 32 (46.88%) | |
| occurrences (all) | 0 | 1 | |
| body aches | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 32 (3.13%) | |
| occurrences (all) | 1 | 1 | |
| early changes of degeneration in spine | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| golfer's elbow | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| hip pain | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 32 (3.13%) | |
| occurrences (all) | 1 | 1 | |
| insertional tendinopathy | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| intermittent bilateral bony elbow pain | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| jaw pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| joint pain | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 2 / 32 (6.25%) | |
| occurrences (all) | 1 | 2 | |
| knee/ankle pain | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 1 / 32 (3.13%) | |
| occurrences (all) | 2 | 1 | |
| leg pain | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| medial epicondylitis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 1 / 32 (3.13%) | |
| occurrences (all) | 2 | 1 | |
| neck strain | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Rheumatoid arthritis/osteoarthritis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 32 (3.13%) | |
| occurrences (all) | 1 | 1 | |
| right glutal tendonitis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| medial foot pain | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sciatic nerve pain | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| shoulder pain | | | |
| subjects affected / exposed | 5 / 59 (8.47%) | 1 / 32 (3.13%) | |
| occurrences (all) | 5 | 1 | |
| finger stiffness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 59 (3.39%) | 0 / 32 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| thigh pain | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| tingling in arms and legs | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| weak joints | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| ankle oedema | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| burn | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| banged knee | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| enlarged heart | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| left leg weakness | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| finger cut | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| left foot injury | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| face pain | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| ear pain | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 1 / 32 (3.13%) | |
| occurrences (all) | 2 | 1 | |
| fever | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 32 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Influenza | | | |
| subjects affected / exposed | 5 / 59 (8.47%) | 0 / 32 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| respiratory infection | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 0 / 32 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Metabolism and nutrition disorders | | | |
| Anorexia nervosa | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 32 (3.13%) | |
| occurrences (all) | 0 | 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

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/32985122