ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: August 31, 2016

ClinicalTrials.gov ID: NCT00545363

Study Identification

Unique Protocol ID:	ML19982
Brief Title:	A Study of Adherence to Once Monthly Ibandronate (Bonviva) in Women With Post-Menopausal Osteoporosis, Supported by a Patient Relationship Program (PRP)
Official Title:	A Randomized Open-Label Study to Investigate the Impact of Bone Marker Feedback at 3 Months on Adherence to Monthly Oral Bonviva in Women With Post-Menopausal Osteoporosis Supported by a Patient Relationship Program
Secondary IDs:	2005-005529-74 [EudraCT Number]

Study Status

Record Verification:	August 2016
Overall Status:	Completed
Study Start:	April 2006
Primary Completion:	January 2008 [Actual]
Study Completion:	January 2008 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 69/02/06 Board Name: Komisija RS za Medicinsko Etico Board Affiliation: NK Phone: +386-1-522-1500 Email: joze.trontelj@kclj.si
Data Monitoring?:	
Plan to Share IPD?:	
Oversight Authorities:	Slovenia: Agencija Republike Slovenije za zdravila in Medicinske Pripomocke

Study Description

Brief Summary:	This 2 arm study will assess the impact of bone marker feedback (BMF), using serum carboxy-terminal collagen crosslinks (CTX) and communication of results at 3 months, on adherence to once monthly ibandronate (150 milligrams [mg] per oral [po]) in women with post-menopausal osteoporosis supported by patient-relationship program (PRP). Participants will be randomized either to receive BMF or no BMF; both groups will be supported by PRP. The anticipated time on study treatment is 3-12 months.
Detailed Description:	

Conditions

Conditions:	Postmenopausal Osteoporosis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 716 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Bone Marker Feedback (BMF) Participants Postmenopausal women will receive ibandronate 150 milligrams (mg) once monthly (QM) orally for 6 months. Participants, in this arm, will receive BMF at Month 3. BMF will be given in terms of providing serum carboxy-terminal collagen crosslinks (CTX) level at Month 3. A "BMF-form" will be provided to the physicians to allow offering the bone marker result in an easy way. Participants will be informed if their results are within or outside of the desired range. In addition, participants will also supported by PRP, to be carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.	Drug: Ibandronate Participants will receive ibandronate 150 mg QM orally for 6 months. Other Names: • Bonviva • Boniva
Active Comparator: No BMF Participants Postmenopausal women will receive ibandronate 150 milligrams (mg) once monthly (QM) orally for 6 months. Participants will be supported by PRP, to be carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.	Drug: Ibandronate Participants will receive ibandronate 150 mg QM orally for 6 months. Other Names: • Bonviva • Boniva

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 55 Years

Maximum Age: 85 Years

Gender: Female

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- ambulatory, post-menopausal women with osteoporosis;
- eligible for bisphosphonate treatment;
- naïve to bisphosphonate therapy, or lapsed users (last bisphosphonate intake greater than or equal to [>=] 6 months ago).

Exclusion Criteria:

- inability to stand or sit upright for at least 60 minutes;

- inability to swallow a tablet whole;
- hypersensitivity to bisphosphonates;
- treatment with drugs, or presence of active disease, known to influence bone metabolism;
- history of upper gastrointestinal disease.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Slovenia
Ljubljana, Slovenia, 1525

Russian Federation
Moscow, Russian Federation, 129110

Moscow, Russian Federation, 117036

Moscow, Russian Federation, 115552

Moscow, Russian Federation, 127299

Moscow, Russian Federation, 117997

Moscow, Russian Federation, 125315

St Petersburg, Russian Federation, 199034

St Petersburg, Russian Federation, 190068

Yaroslavl, Russian Federation, 150003

Ekaterinburg, Russian Federation, 620102

Moscow, Russian Federation, 101990

Hungary
Budapest, Hungary, 1027

Budapest, Hungary, 1113

Szeged, Hungary, 6720

Békéscsaba, Hungary, 5600

Miskolc, Hungary, 3529

Szekesfehervar, Hungary, 8000

Szombathely, Hungary, 9700

Pecs, Hungary, 7624

Debrecen, Hungary, 4043

Budapest, Hungary, 1032

Slovakia
Bratislava, Slovakia, 826 06

Lubochna, Slovakia, 034 91

Piestany, Slovakia, 921 12

Russian Federation
Moscow, Russian Federation, 127473

Moscow, Russian Federation, 117997

Slovakia
Banska Bystrica, Slovakia, 975 17

Russian Federation
Moscow, Russian Federation, 111123

Irkutsk, Russian Federation, 664047

St Petersburg, Russian Federation, 199034

Slovakia
Presov, Slovakia, 080 01

Romania
Timisoara, Romania, 300736

Constanta, Romania, 900709

Bucharest, Romania, 011172

Craiova, Romania, 300941

Cluj-napoca, Romania, 400006

Poland
Krakow, Poland, 30-510

Poznan, Poland, 60-355

Warszawa, Poland, 00-719

Wroclaw, Poland, 50-367

Gliwice, Poland, 44-100

Warszawa, Poland, 02-637

Lodz, Poland, 90-549

Warszawa, Poland, 00-909

Warszawa, Poland, 02-507

Latvia
Riga, Latvia, 1038

Riga, Latvia, 1004

Riga, Latvia, LV-1012

Liepaja, Latvia, 3400

Romania
Bucharest, Romania, 011364

Bucharest, Romania, 011461

Bucharest, Romania, 011863

Russian Federation
Voronezh, Russian Federation, 394066

Voronezh, Russian Federation, 394066

References

Citations:

Links:

Study Results

Participant Flow

Reporting Groups

	Description
Bone Marker Feedback (BMF) Participants	Postmenopausal women received ibandronate 150 milligrams (mg) once monthly (QM) orally for 6 months. Participants, in this arm, received bone marker feedback (BMF) at Month 3. BMF was given in terms of providing serum carboxy-terminal collagen crosslinks (CTX) level at Month 3. A "BMF-form" was provided to the physicians to allow offering the bone marker result in an easy way. Participants were informed that their results were within or outside of the desired range. In addition, participants were also supported by patient relationship program (PRP), carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.
No BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants were supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.

Overall Study

	Bone Marker Feedback (BMF) Participants	No BMF Participants
Started	358	358
Treated	354	357
Completed	339	343
Not Completed	19	15
Adverse Event	6	7
Withdrawal by Subject	6	5
Non-compliance	3	1
Did not meet entry criteria	1	1

	Bone Marker Feedback (BMF) Participants	No BMF Participants
Lost to Follow-up	2	0
Unspecified	1	1

Baseline Characteristics

Baseline Analysis Population Description

Safety population included participants who received at least 1 dose of study drug.

Reporting Groups

	Description
BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants, in this arm, received BMF at Month 3. BMF was given in terms of providing serum CTX level at Month 3. A "BMF-form" was provided to the physicians to allow offering the bone marker result in an easy way. Participants were informed that their results were within or outside of the desired range. In addition, participants were also supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.
No BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants were supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.

Baseline Measures

		BMF Participants	No BMF Participants	Total
Overall Number of Participants		354	357	711
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	354 participants	357 participants	711 participants
		66.7 (7.12)	65.6 (6.64)	66.2 (6.90)
Gender, Male/ Female Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	354 participants	357 participants	711 participants
	Female	354 100%	357 100%	711 100%
	Male	0 0%	0 0%	0 0%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Adherence to Treatment
Measure Description	Participants were considered adherent to treatment if they took at least 83 percent (%) of their assigned medications (5 of the 6 monthly ibandronate tablets) within the -1 to +21 days of their osteoporosis treatment date each month. Participant adherence was assessed by maintaining records of ‘drug dispensed’ and ‘drug returned’ on case report form (CRF) and participant’s self-report on Visit 2 (Month 3) and final study visit (Month 6). A drug dispensing log was maintained by the investigator. Participants were instructed at the baseline visit and Visit 2 to save and return unused or partially used medication packages on Visit 2 and final study visit, respectively.
Time Frame	Up to 6 months
Safety Issue?	No

Analysis Population Description

Intent to treat (ITT) population included all randomized participants. Number of participants analyzed=number of participants evaluable for this outcome.

Reporting Groups

	Description
BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants, in this arm, received BMF at Month 3. BMF was given in terms of providing serum CTX level at Month 3. A "BMF-form” was provided to the physicians to allow offering the bone marker result in an easy way. Participants were informed that their results were within or outside of the desired range. In addition, participants were also supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant’s regular drug intake.
No BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants were supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant’s regular drug intake.

Measured Values

	BMF Participants	No BMF Participants
Number of Participants Analyzed	271	284
Percentage of Participants With Adherence to Treatment Measure Type: Number Unit of measure: percentage of participants	98.5	98.6

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Osteoporosis Patient Satisfaction Questionnaire (OPSAT-Q) Composite Satisfaction High Scores
Measure Description	The OPSAT-Q is a validated questionnaire designed to capture satisfaction with bisphosphonate treatment. It comprises four domains: convenience (questions 1 - 6), quality of life (questions 7 and 8), overall satisfaction (questions 9 and 10), and side effects (questions 11 - 16). Satisfaction with treatment was assessed using the OPSAT-Q composite satisfaction score, which was the average of the scores from the four domains of the OPSAT-Q converted to a 0 - 100-point scale. Higher scores indicated greater treatment satisfaction. A score of 80 or more was considered as high score.
Time Frame	At Month 6
Safety Issue?	No

Analysis Population Description

ITT population. Number of participants analyzed = participants evaluable for this outcome.

Reporting Groups

	Description
BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants, in this arm, received BMF at Month 3. BMF was given in terms of providing serum CTX level at Month 3. A "BMF-form" was provided to the physicians to allow offering the bone marker result in an easy way. Participants were informed that their results were within or outside of the desired range. In addition, participants were also supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.
No BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants were supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.

Measured Values

	BMF Participants	No BMF Participants
Number of Participants Analyzed	328	336
Percentage of Participants With Osteoporosis Patient Satisfaction Questionnaire (OPSAT-Q) Composite Satisfaction High Scores Measure Type: Number Unit of measure: percentage of participants	87.72	87.62

Statistical Analysis 1 for Percentage of Participants With Osteoporosis Patient Satisfaction Questionnaire (OPSAT-Q) Composite Satisfaction High Scores

Statistical Analysis Overview	Comparison Groups	BMF Participants, No BMF Participants
	Comments	Statistical analysis was done to compare the participant satisfaction between the Biofeedback and No-feedback arms.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	=0.8989
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Osteoporosis Patient Perception Survey (OPPS) and Osteoporosis Medical Care Satisfaction Questionnaire (OMSQ) Composite Satisfaction High Score
Measure Description	OPPS: A standardized 6-item satisfaction questionnaire for osteoporosis medical care and treatment received during the study. Individual item score was transformed and converted to a 0 to 100 scale where higher score indicated greater satisfaction. The composite score was the average of individual item scores (transformed) and ranged from 0 to 100, where higher scores indicated greater satisfaction. OMSQ: A standardized 18-item satisfaction questionnaire for osteoporosis medical care, treatment received and blood test and their results during the study. Individual item score was transformed and converted to a 0 to 100 scale where higher score indicated greater satisfaction. The composite score was the average of individual item scores (transformed) and ranged from 0 to 100, where higher scores indicated greater satisfaction.
Time Frame	At Month 6
Safety Issue?	No

Analysis Population Description

ITT population. Number of participants analyzed = participants evaluable for this outcome.

Reporting Groups

	Description
BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants, in this arm, received BMF at Month 3. BMF was given in terms of providing serum CTX level at Month 3. A "BMF-form" was provided to the physicians to allow offering the bone marker result in an easy way. Participants were informed that their results were within or outside of the desired range. In addition, participants were also supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.
No BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants were supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.

Measured Values

	BMF Participants	No BMF Participants
Number of Participants Analyzed	328	334
Percentage of Participants With Osteoporosis Patient Perception Survey (OPPS) and Osteoporosis Medical Care Satisfaction Questionnaire (OMSQ) Composite Satisfaction High Score Measure Type: Number Unit of measure: percentage of participants	74.9	72.2

Statistical Analysis 1 for Percentage of Participants With Osteoporosis Patient Perception Survey (OPPS) and Osteoporosis Medical Care Satisfaction Questionnaire (OMSQ) Composite Satisfaction High Score

Statistical Analysis Overview	Comparison Groups	BMF Participants, No BMF Participants
	Comments	Statistical analysis was done to compare the participant perception between the Biofeedback and No-feedback arms.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	=0.453
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in CTX Based on Adherence to Ibandronate
Measure Description	Serum CTX, a biochemical marker of bone resorption, was assessed for all participants at baseline and at final visit (Month 6). The sampling was done at the same time of the day each time to overcome the effect of circadian fluctuations. Participants were considered adherent to treatment if they took at least 83% of their assigned medications (5 of the 6 monthly ibandronate tablets) within the -1 to +21 days of their osteoporosis treatment date each month. Participant adherence was assessed by maintaining records of 'drug dispensed' and 'drug returned' on CRF and participant's self-report on Visit 2 (Month 3) and final study visit (Month 6). A drug dispensing log was maintained by the investigator. Participants were instructed at the baseline visit and Visit 2 to save and return unused or partially used medication packages on Visit 2 and final study visit, respectively.
Time Frame	Baseline, Month 6
Safety Issue?	No

Analysis Population Description

ITT population. Number of participants analyzed = participants evaluable for this outcome and "n" represents number of participants analyzed for the specified category.

Reporting Groups

	Description
BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants, in this arm, received BMF at Month 3. BMF was given in terms of providing serum CTX level at Month 3. A "BMF-form" was provided to the physicians to allow offering the bone marker result in an easy way. Participants were informed that their results were within or outside of the desired range. In addition, participants were also supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.
No BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants were supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.

Measured Values

	BMF Participants	No BMF Participants
Number of Participants Analyzed	280	287
Percent Change From Baseline in CTX Based on Adherence to Ibandronate Least Squares Mean (95% Confidence Interval) Unit of measure: percent change		

	BMF Participants	No BMF Participants
Adherence-Yes (n=279, 281)	-47.5 (-51.3 to -43.5)	-47.5 (-51.0 to -43.9)
Adherence-No (n=1, 6)	-71.74 (NA to NA) [1]	-25.8 (-91.0 to 13.5)

[1] Standard deviation is not applicable as there is only 1 participant.

Statistical Analysis 1 for Percent Change From Baseline in CTX Based on Adherence to Ibandronate

Statistical Analysis Overview	Comparison Groups	BMF Participants, No BMF Participants
	Comments	Statistical analysis was done to compare the effect of adherence (Yes/No) on percent change from baseline in CTX between the Biofeedback and No-feedback arms.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	=0.4917
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

Reported Adverse Events

Time Frame	15-30 days after final visit (final visit=up to 6 months)
Additional Description	[Not specified]

Reporting Groups

	Description
BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants, in this arm, received BMF at Month 3. BMF was given in terms of providing serum CTX level at Month 3. A "BMF-form" was provided to the physicians to allow offering the bone marker result in an easy way. Participants were informed that their results were within or outside of the desired range. In addition, participants were also supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.

	Description
No BMF Participants	Postmenopausal women received ibandronate 150 mg QM orally for 6 months. Participants were supported by PRP, carried out by supplying alarm devices, specifically designed to support the participant's regular drug intake.

Serious Adverse Events

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Total	8/354 (2.26%)	5/357 (1.4%)
Cardiac disorders		
Cardiac arrest [A] *	1/354 (0.28%)	0/357 (0%)
Myocardial infarction [A] *	0/354 (0%)	1/357 (0.28%)
Sinus arrhythmia [A] *	1/354 (0.28%)	0/357 (0%)
Gastrointestinal disorders		
Colitis ulcerative [A] *	0/354 (0%)	1/357 (0.28%)
General disorders		
Sudden death [A] *	1/354 (0.28%)	0/357 (0%)
Infections and infestations		
Appendicitis [A] *	1/354 (0.28%)	0/357 (0%)
Hepatitis C [A] *	0/354 (0%)	1/357 (0.28%)
Pneumonia [A] *	1/354 (0.28%)	0/357 (0%)
Musculoskeletal and connective tissue disorders		
Osteonecrosis [A] *	0/354 (0%)	1/357 (0.28%)
Nervous system disorders		
Headache [A] *	1/354 (0.28%)	0/357 (0%)
Loss of consciousness [A] *	0/354 (0%)	1/357 (0.28%)
Vascular encephalopathy [A] *	1/354 (0.28%)	0/357 (0%)
Surgical and medical procedures		

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Cholecystectomy [A] *	1/354 (0.28%)	0/357 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (19.0)

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Total	196/354 (55.37%)	224/357 (62.75%)
Blood and lymphatic system disorders		
Anaemia [A] *	0/354 (0%)	2/357 (0.56%)
Thrombocytopenia [A] *	1/354 (0.28%)	0/357 (0%)
Cardiac disorders		
Palpitations [A] *	1/354 (0.28%)	0/357 (0%)
Tachycardia [A] *	3/354 (0.85%)	0/357 (0%)
Tricuspid valve disease [A] *	1/354 (0.28%)	0/357 (0%)
Ear and labyrinth disorders		
Vertigo [A] *	2/354 (0.56%)	1/357 (0.28%)
Eye disorders		
Cataract [A] *	0/354 (0%)	1/357 (0.28%)
Conjunctival hyperaemia [A] *	0/354 (0%)	1/357 (0.28%)
Eye pain [A] *	1/354 (0.28%)	0/357 (0%)
Keratopathy [A] *	0/354 (0%)	1/357 (0.28%)
Visual impairment [A] *	1/354 (0.28%)	0/357 (0%)
Gastrointestinal disorders		

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Abdominal discomfort [A] *	1/354 (0.28%)	0/357 (0%)
Abdominal pain [A] *	6/354 (1.69%)	4/357 (1.12%)
Abdominal pain upper [A] *	5/354 (1.41%)	9/357 (2.52%)
Abnormal faeces [A] *	0/354 (0%)	1/357 (0.28%)
Constipation [A] *	1/354 (0.28%)	1/357 (0.28%)
Diarrhoea [A] *	9/354 (2.54%)	12/357 (3.36%)
Diverticulum intestinal [A] *	0/354 (0%)	1/357 (0.28%)
Dry mouth [A] *	0/354 (0%)	1/357 (0.28%)
Dyspepsia [A] *	4/354 (1.13%)	10/357 (2.8%)
Epigastric discomfort [A] *	1/354 (0.28%)	0/357 (0%)
Gastritis [A] *	2/354 (0.56%)	1/357 (0.28%)
Gastritis erosive [A] *	0/354 (0%)	1/357 (0.28%)
Gastrooesophageal reflux disease [A] *	2/354 (0.56%)	2/357 (0.56%)
Glossitis [A] *	0/354 (0%)	1/357 (0.28%)
Glossodynia [A] *	0/354 (0%)	2/357 (0.56%)
Haemorrhoidal haemorrhage [A] *	0/354 (0%)	1/357 (0.28%)
Haemorrhoids [A] *	0/354 (0%)	1/357 (0.28%)
Nausea [A] *	10/354 (2.82%)	5/357 (1.4%)
Oesophagitis [A] *	0/354 (0%)	1/357 (0.28%)
Oral discomfort [A] *	1/354 (0.28%)	0/357 (0%)
Pancreatic disorder [A] *	1/354 (0.28%)	0/357 (0%)
Pancreatitis chronic [A] *	0/354 (0%)	1/357 (0.28%)

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Toothache [A] *	0/354 (0%)	1/357 (0.28%)
Vomiting [A] *	1/354 (0.28%)	1/357 (0.28%)
General disorders		
Acute phase reaction [A] *	1/354 (0.28%)	0/357 (0%)
Asthenia [A] *	0/354 (0%)	1/357 (0.28%)
Chest pain [A] *	1/354 (0.28%)	1/357 (0.28%)
Chills [A] *	1/354 (0.28%)	1/357 (0.28%)
Fatigue [A] *	0/354 (0%)	2/357 (0.56%)
Hyperthermia [A] *	0/354 (0%)	1/357 (0.28%)
Influenza like illness [A] *	4/354 (1.13%)	1/357 (0.28%)
Malaise [A] *	1/354 (0.28%)	1/357 (0.28%)
Pyrexia [A] *	2/354 (0.56%)	0/357 (0%)
Hepatobiliary disorders		
Biliary colic [A] *	0/354 (0%)	2/357 (0.56%)
Hepatic pain [A] *	1/354 (0.28%)	0/357 (0%)
Immune system disorders		
Food allergy [A] *	1/354 (0.28%)	0/357 (0%)
Infections and infestations		
Abscess [A] *	0/354 (0%)	1/357 (0.28%)
Bronchitis [A] *	3/354 (0.85%)	5/357 (1.4%)
Cellulitis [A] *	0/354 (0%)	1/357 (0.28%)
Conjunctivitis [A] *	1/354 (0.28%)	0/357 (0%)
Cystitis [A] *	5/354 (1.41%)	3/357 (0.84%)

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Fungal infection [A] *	0/354 (0%)	1/357 (0.28%)
Gastroenteritis [A] *	0/354 (0%)	1/357 (0.28%)
Herpes zoster [A] *	2/354 (0.56%)	0/357 (0%)
Influenza [A] *	3/354 (0.85%)	4/357 (1.12%)
Nasopharyngitis [A] *	6/354 (1.69%)	10/357 (2.8%)
Otitis media [A] *	0/354 (0%)	1/357 (0.28%)
Pharyngitis [A] *	3/354 (0.85%)	4/357 (1.12%)
Pneumonia [A] *	0/354 (0%)	2/357 (0.56%)
Pyelonephritis [A] *	1/354 (0.28%)	0/357 (0%)
Respiratory tract infection [A] *	1/354 (0.28%)	1/357 (0.28%)
Respiratory tract infection viral [A] *	0/354 (0%)	1/357 (0.28%)
Sinusitis [A] *	0/354 (0%)	2/357 (0.56%)
Upper respiratory tract infection [A] *	1/354 (0.28%)	1/357 (0.28%)
Urinary tract infection [A] *	6/354 (1.69%)	4/357 (1.12%)
Viral infection [A] *	0/354 (0%)	2/357 (0.56%)
Viral upper respiratory tract infection [A] *	0/354 (0%)	1/357 (0.28%)
Injury, poisoning and procedural complications		
Burn oesophageal [A] *	1/354 (0.28%)	0/357 (0%)
Forearm fracture [A] *	2/354 (0.56%)	0/357 (0%)
Fracture [A] *	2/354 (0.56%)	1/357 (0.28%)
Humerus fracture [A] *	0/354 (0%)	1/357 (0.28%)
Ligament sprain [A] *	3/354 (0.85%)	1/357 (0.28%)

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Limb injury [A] *	0/354 (0%)	1/357 (0.28%)
Lower limb fracture [A] *	0/354 (0%)	1/357 (0.28%)
Near drowning [A] *	1/354 (0.28%)	0/357 (0%)
Wound haemorrhage [A] *	0/354 (0%)	1/357 (0.28%)
Wrist fracture [A] *	0/354 (0%)	1/357 (0.28%)
Investigations		
Blood creatinine increased [A] *	1/354 (0.28%)	1/357 (0.28%)
Blood glucose increased [A] *	2/354 (0.56%)	1/357 (0.28%)
Blood phosphorus decreased [A] *	0/354 (0%)	1/357 (0.28%)
Blood potassium decreased [A] *	0/354 (0%)	1/357 (0.28%)
Laboratory test abnormal [A] *	1/354 (0.28%)	0/357 (0%)
Urine output increased [A] *	1/354 (0.28%)	0/357 (0%)
Metabolism and nutrition disorders		
Diabetes mellitus [A] *	1/354 (0.28%)	0/357 (0%)
Dyslipidaemia [A] *	1/354 (0.28%)	0/357 (0%)
Gout [A] *	0/354 (0%)	1/357 (0.28%)
Hypercholesterolaemia [A] *	0/354 (0%)	1/357 (0.28%)
Hyperglycaemia [A] *	1/354 (0.28%)	1/357 (0.28%)
Hyperlipidaemia [A] *	1/354 (0.28%)	0/357 (0%)
Hypocalcaemia [A] *	1/354 (0.28%)	2/357 (0.56%)
Hypophosphataemia [A] *	0/354 (0%)	1/357 (0.28%)
Lipid metabolism disorder [A] *	0/354 (0%)	1/357 (0.28%)
Metabolic disorder [A] *	1/354 (0.28%)	0/357 (0%)

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	11/354 (3.11%)	11/357 (3.08%)
Arthritis [A] *	1/354 (0.28%)	0/357 (0%)
Back pain [A] *	8/354 (2.26%)	13/357 (3.64%)
Bone pain [A] *	3/354 (0.85%)	3/357 (0.84%)
Joint stiffness [A] *	0/354 (0%)	1/357 (0.28%)
Metatarsalgia [A] *	1/354 (0.28%)	0/357 (0%)
Muscular weakness [A] *	1/354 (0.28%)	0/357 (0%)
Musculoskeletal chest pain [A] *	0/354 (0%)	1/357 (0.28%)
Musculoskeletal pain [A] *	3/354 (0.85%)	4/357 (1.12%)
Myalgia [A] *	2/354 (0.56%)	7/357 (1.96%)
Neck pain [A] *	1/354 (0.28%)	3/357 (0.84%)
Osteoarthritis [A] *	1/354 (0.28%)	2/357 (0.56%)
Osteochondrosis [A] *	1/354 (0.28%)	1/357 (0.28%)
Pain in extremity [A] *	5/354 (1.41%)	1/357 (0.28%)
Pain in jaw [A] *	2/354 (0.56%)	2/357 (0.56%)
Spinal osteoarthritis [A] *	0/354 (0%)	1/357 (0.28%)
Nervous system disorders		
Cerebral infarction [A] *	1/354 (0.28%)	0/357 (0%)
Cerebrovascular disorder [A] *	0/354 (0%)	1/357 (0.28%)
Cervicobrachial syndrome [A] *	1/354 (0.28%)	0/357 (0%)
Disturbance in attention [A] *	1/354 (0.28%)	0/357 (0%)
Dizziness [A] *	1/354 (0.28%)	1/357 (0.28%)

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Dysgeusia [A] *	1/354 (0.28%)	1/357 (0.28%)
Headache [A] *	4/354 (1.13%)	7/357 (1.96%)
Migraine [A] *	0/354 (0%)	1/357 (0.28%)
Neuralgia [A] *	0/354 (0%)	1/357 (0.28%)
Paraesthesia [A] *	1/354 (0.28%)	0/357 (0%)
Polyneuropathy [A] *	0/354 (0%)	1/357 (0.28%)
Somnolence [A] *	0/354 (0%)	1/357 (0.28%)
Vertebrobasilar insufficiency [A] *	0/354 (0%)	1/357 (0.28%)
Psychiatric disorders		
Anxiety disorder [A] *	1/354 (0.28%)	0/357 (0%)
Depression [A] *	1/354 (0.28%)	1/357 (0.28%)
Hallucination [A] *	0/354 (0%)	1/357 (0.28%)
Insomnia [A] *	1/354 (0.28%)	1/357 (0.28%)
Panic disorder [A] *	1/354 (0.28%)	1/357 (0.28%)
Renal and urinary disorders		
Calculus urinary [A] *	2/354 (0.56%)	0/357 (0%)
Dysuria [A] *	1/354 (0.28%)	0/357 (0%)
Renal colic [A] *	0/354 (0%)	1/357 (0.28%)
Respiratory, thoracic and mediastinal disorders		
Acute respiratory failure [A] *	0/354 (0%)	1/357 (0.28%)
Cough [A] *	0/354 (0%)	1/357 (0.28%)
Dyspnoea [A] *	1/354 (0.28%)	1/357 (0.28%)
Interstitial lung disease [A] *	1/354 (0.28%)	0/357 (0%)

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Laryngeal pain [A] *	2/354 (0.56%)	0/357 (0%)
Lung disorder [A] *	1/354 (0.28%)	0/357 (0%)
Rhinitis allergic [A] *	0/354 (0%)	1/357 (0.28%)
Throat irritation [A] *	1/354 (0.28%)	0/357 (0%)
Skin and subcutaneous tissue disorders		
Alopecia [A] *	1/354 (0.28%)	1/357 (0.28%)
Dermatitis [A] *	1/354 (0.28%)	0/357 (0%)
Dermatitis allergic [A] *	1/354 (0.28%)	0/357 (0%)
Pruritus [A] *	1/354 (0.28%)	1/357 (0.28%)
Rash [A] *	1/354 (0.28%)	1/357 (0.28%)
Urticaria [A] *	0/354 (0%)	1/357 (0.28%)
Surgical and medical procedures		
Glaucoma surgery [A] *	0/354 (0%)	1/357 (0.28%)
Hip arthroplasty [A] *	0/354 (0%)	1/357 (0.28%)
Hysterectomy [A] *	1/354 (0.28%)	0/357 (0%)
Tooth extraction [A] *	1/354 (0.28%)	1/357 (0.28%)
Vascular disorders		
Arteriosclerosis [A] *	2/354 (0.56%)	0/357 (0%)
Hypertension [A] *	4/354 (1.13%)	4/357 (1.12%)
Labile blood pressure [A] *	0/354 (0%)	1/357 (0.28%)
Orthostatic hypotension [A] *	1/354 (0.28%)	0/357 (0%)
Phlebitis [A] *	0/354 (0%)	1/357 (0.28%)
Varicose vein [A] *	1/354 (0.28%)	0/357 (0%)

	BMF Participants	No BMF Participants
	Affected/At Risk (%)	Affected/At Risk (%)
Venous thrombosis [A] *	0/354 (0%)	1/357 (0.28%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (19.0)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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