ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 04/05/2016

ClinicalTrials.gov ID: NCT00545051

Study Identification

Unique Protocol ID:	ML20088
Brief Title:	A Study of Once Monthly Bonviva (Ibandronate) in Prevention of Glucocorticoid-Induced Osteoporosis.
Official Title:	A Randomized, Double-blind Study to Evaluate the Effect of Once Monthly Bonviva on Lumbar Bone Mineral Density in the Prevention of Glucocorticoid-induced Osteoporosis in Post-menopausal Women
Secondary IDs:	

Study Status

Record Verification:	April 2016
Overall Status:	Completed
Study Start:	May 2006
Primary Completion:	May 2009 [Actual]
Study Completion:	May 2009 [Actual]

Sponsor/Collaborators

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

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: 176/2006 Board Name: HUS Sisatautien eettinen toimikunta Board Affiliation: unknown Phone: +358 9 47171484 Email: eetiset.toimikunnat@hus.fi
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Finland: Ministry of Social Affairs and Health/ETENE

Study Description

Brief Summary:	This 2 arm study will investigate the efficacy and safety of Bonviva (150mg po monthly) in the prevention of glucocorticoid-induced osteoporosis in post-menopausal women. Patients will be randomized to receive either Bonviva 150mg po or placebo monthly, with vitamin D and calcium supplementation. The anticipated time on study treatment is 1-2 years, and the target sample size is 100-500 individuals.
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:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	140 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Ibandronate Participants received monthly oral ibandronate (150 milligrams [mg]) for 12 months.	Drug: ibandronate 150mg po monthly for 12 months Other Names: • Bonviva/Boniva
Placebo Comparator: Placebo Participants received monthly oral placebo for 12 months.	Drug: Placebo po monthly for 12 months

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 50 Years

Maximum Age: 85 Years

Gender: Female

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- post-menopausal women, 50-85 years of age;
- any inflammatory rheumatoid disease including polymyalgia rheumatica;
- receiving treatment with 5-15 mg/day of prednisolone.

Exclusion Criteria:

- previous treatment with an iv bisphosphonate at any time;
- previous treatment with an oral bisphosphonate within the last 6 months, >1 month of treatment within last year, or >3 months of treatment within last 2 years;
- treatment with parathyroid hormone in last 2 years;
- inability to stand or sit in an upright position for at least 60 minutes;
- inability to swallow a tablet whole;
- history of major gastrointestinal disease.

Contacts/Locations

Study Officials: Clinical Trials
Study Director

Hoffmann-La Roche

Locations: Finland

Lahti, Finland, 15110

Helsinki, Finland, 00290

Helsinki, Finland, 00100

Tampere, Finland, 33100

Turku, Finland, 20100

Oulu, Finland, 90029

Hyvinkää, Finland, 05800

Vantaa, Finland, 01300

Hämeenlinna, Finland, 13530

Kuopio, Finland, 70211

Tampere, Finland, 33101

Jyvaeskylae, Finland, 10100

Jyväskylä, Finland, 40100

Oulu, Finland, 90100

Helsinki, Finland, 00350

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Ibandronate	Participants received 150 milligram (mg) ibandronate tablet orally once a month for 12 months. Participants also received 1000 mg calcium and 800 International Units (IU) Vitamin D per day.
Placebo	Participants received oral placebo tablet once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.

Overall Study

	Ibandronate	Placebo
Started	68	72
Completed	59	65
Not Completed	9	7
Adverse Event	7	3
Death	1	0
Violation of inclusion/exclusion	0	2
Protocol Violation	1	0
Withdrawal by Subject	0	1
Administrative reasons	0	1

Baseline Characteristics

Analysis Population Description

The intent-to-treat (ITT) population included all participants randomized and who had at least one follow up efficacy data time point available.

Reporting Groups

	Description
Ibandronate	Participants received 150 mg ibandronate tablet orally once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.
Placebo	Participants received oral placebo tablet once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.

Baseline Measures

	Ibandronate	Placebo	Total
Number of Participants	68	72	140
Age, Continuous [units: years] Mean (Standard Deviation)	64.4 (7.90)	63.2 (6.83)	63.79 (7.39)
Gender, Male/Female [units: participants]			
Female	68	72	140
Male	0	0	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percent Change From Baseline in Mean Lumbar Spine Bone Mineral Density (BMD) at Month 12
Measure Description	Lumbar spine BMD was measured at Baseline, and Months 6 and 12 using dual-energy x-ray absorptiometry (DXA). Percent change from Baseline to Month 12 was calculated using analysis of covariance.
Time Frame	Baseline and Month 12
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population

Reporting Groups

	Description
Ibandronate	Participants received 150 mg ibandronate tablet orally once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.
Placebo	Participants received oral placebo tablet once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.

Measured Values

	Ibandronate	Placebo
Number of Participants Analyzed	66	66
Percent Change From Baseline in Mean Lumbar Spine Bone Mineral Density (BMD) at Month 12	3.2 (3.7)	-0.1 (3.0)

	Ibandronate	Placebo
[units: percent change in BMD] Mean (Standard Deviation)		

Statistical Analysis 1 for Percent Change From Baseline in Mean Lumbar Spine Bone Mineral Density (BMD) at Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	3.25
	Confidence Interval	(2-Sided) 95% 2.09 to 4.41
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Mean Lumbar Spine BMD at Month 6
Measure Description	Lumbar spine BMD was measured at Baseline and Month 6 using DXA. Percent change from Baseline to Month 6 was calculated using analysis of covariance.
Time Frame	Baseline and Month 6
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Ibandronate	Participants received 150 mg ibandronate tablet orally once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.
Placebo	Participants received oral placebo tablet once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.

Measured Values

	Ibandronate	Placebo
Number of Participants Analyzed	62	66
Percent Change From Baseline in Mean Lumbar Spine BMD at Month 6 [units: percent change in BMD] Mean (Standard Deviation)	2.6 (3.1)	0.3 (2.8)

Statistical Analysis 1 for Percent Change From Baseline in Mean Lumbar Spine BMD at Month 6

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	2.22
	Confidence Interval	(2-Sided) 95% 1.22 to 3.23
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Mean Total Hip BMD at Month 6 and Month 12
Measure Description	Left total hip BMD was measured by DXA at Baseline, and Months 6 and 12. If there was prosthesis of left hip, the measurement of right total hip BMD was done by DXA. Percent change from Baseline to Months 6 and 12 was calculated using analysis of (co)variance for repeated measurements.
Time Frame	Baseline and Months 6 and 12
Safety Issue?	No

Analysis Population Description

ITT population; number (n) equals (=) number of participants analyzed at the specified visit.

Reporting Groups

	Description
Ibandronate	Participants received 150 mg ibandronate tablet orally once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.
Placebo	Participants received oral placebo tablet once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.

Measured Values

	Ibandronate	Placebo
Number of Participants Analyzed	66	66
Percent Change From Baseline in Mean Total Hip BMD at Month 6 and Month 12 [units: percent change in BMD] Mean (Standard Deviation)		
Month 6 (n=62,66)	0.7 (1.9)	0.0 (2.1)
Month 12 (n=66,65)	1.2 (2.2)	-0.7 (2.5)

Statistical Analysis 1 for Percent Change From Baseline in Mean Total Hip BMD at Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	Month 6
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.122
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.55
	Confidence Interval	(2-Sided) 95% -0.15 to 1.25
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Percent Change From Baseline in Mean Total Hip BMD at Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	Month 12
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	1.81
	Confidence Interval	(2-Sided) 95% 0.96 to 2.66
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Measure Description	Serum C-terminal Telopeptide of Type 1 Collagen (sCTX), Serum Procollagen Type 1 N-terminal Propeptide (P1NP) and Serum Bone Tartrate-resistant Acid Phosphatase Isoform 5b (TRACP) are measures of bone resorption and are measured as nanograms per milliliter (ng/mL). Percent change from Baseline to Months 1, 6 and 12 was calculated using analysis of covariance for repeated measurements.
Time Frame	Baseline and Months 1, 6 and 12
Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants analyzed at the specified visit for the given parameter.

Reporting Groups

	Description
Ibandronate	Participants received 150 mg ibandronate tablet orally once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.
Placebo	Participants received oral placebo tablet once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.

Measured Values

	Ibandronate	Placebo
Number of Participants Analyzed	68	68
Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12 [units: percent change in bone turnover markers] Mean (Standard Deviation)		
sCTX Month 1 (n=68,68)	-44.7 (36.5)	-3.8 (33.3)
sCTX Month 6 (n=62,66)	-53.3 (24.3)	-3.5 (48.0)
sCTX Month 12 (n=65,65)	-42.0 (27.9)	11.6 (82.4)
P1NP Month 1 (n=68,68)	-23.8 (17.2)	-2.3 (22.5)
P1NP Month 6 (n=60,66)	-62.5 (16.3)	-3.7 (44.5)
P1NP Month 12 (n=64,67)	-48.8 (37.2)	12.5 (54.6)
TRACP Month 1 (n=68,68)	-31.3 (12.0)	-7.3 (11.9)
TRACP Month 6 (n=62,66)	-32.9 (14.8)	-7.1 (17.0)
TRACP Month 12 (n=65,67)	-27.4 (16.5)	-6.3 (18.0)

Statistical Analysis 1 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	sCTX at Month 1
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Statistical Analysis 2 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	sCTX at Month 6
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Statistical Analysis 3 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	sCTX at Month 12
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Statistical Analysis 4 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	P1NP at Month 1
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Statistical Analysis 5 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	P1NP at Month 6
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Statistical Analysis 6 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	P1NP at Month 12

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Statistical Analysis 7 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	TRACP at Month 1
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Statistical Analysis 8 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	TRACP at Month 6
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Statistical Analysis 9 for Percent Change From Baseline in Bone Turnover Markers at Month 1, Month 6 and Month 12

Statistical Analysis Overview	Comparison Groups	Ibandronate, Placebo
	Comments	TRACP at Month 12
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Withdrawn Due to Worsening in BMD at 6 Months and/or Worsening in BMD at Least 7 Percent (%) at Any Site at 6 Months
Measure Description	Worsening in BMD was defined as BMD T-score at any site less than or equal to (≤) - 2.5 standard deviations and/or worsening in BMD of at least 7% at any site.
Time Frame	Month 6
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Ibandronate	Participants received 150 mg ibandronate tablet orally once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.
Placebo	Participants received oral placebo tablet once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.

Measured Values

	Ibandronate	Placebo
Number of Participants Analyzed	62	66

	Ibandronate	Placebo
Percentage of Participants Withdrawn Due to Worsening in BMD at 6 Months and/or Worsening in BMD at Least 7 Percent (%) at Any Site at 6 Months [units: percentage of participants]	0.0	0.0

Reported Adverse Events

Time Frame	Adverse events were collected from the date of randomization until 15 days after the end of study at 12 months.
Additional Description	The safety population included all participants who had at least one dose of the trial medication, whether withdrawn prematurely or not, and at least one follow-up data point. Two participants received both treatments and were allocated to the ibandronate group for all assessments of safety.

Reporting Groups

	Description
Ibandronate	Participants received 150 mg ibandronate tablet orally once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.
Placebo	Participants received oral placebo tablet once a month for 12 months. Participants also received 1000 mg calcium and 800 IU Vitamin D per day.

Serious Adverse Events

	Ibandronate	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	10/70 (14.29%)	6/70 (8.57%)
Blood and lymphatic system disorders		
Agranulocytosis [A] *	1/70 (1.43%)	0/70 (0%)
Anaemia due to gastrointestinal bleeding [A] *	1/70 (1.43%)	0/70 (0%)
Deep vein thrombosis [A] *	2/70 (2.86%)	0/70 (0%)
General disorders		
Concussion [A] *	1/70 (1.43%)	0/70 (0%)

	Ibandronate	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Infections and infestations		
Acute pancreatitis [A] *	1/70 (1.43%)	0/70 (0%)
Acute pyelonephritis [A] *	1/70 (1.43%)	0/70 (0%)
Erysipelas [A] *	0/70 (0%)	1/70 (1.43%)
Pneumonia [A] *	0/70 (0%)	1/70 (1.43%)
Sepsis [A] *	1/70 (1.43%)	0/70 (0%)
Injury, poisoning and procedural complications		
Hip fracture [A] *	0/70 (0%)	1/70 (1.43%)
Radius fracture [A] *	0/70 (0%)	1/70 (1.43%)
Investigations		
Poisoning [A] *	1/70 (1.43%)	0/70 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Follicle centre lymphoma [A] *	1/70 (1.43%)	0/70 (0%)
Malignant tongue neoplasm [A] *	1/70 (1.43%)	0/70 (0%)
Nervous system disorders		
Headache [A] *	0/70 (0%)	2/70 (2.86%)
Transient ischaemic attack [A] *	1/70 (1.43%)	0/70 (0%)
Respiratory, thoracic and mediastinal disorders		
Pulmonary embolism [A] *	1/70 (1.43%)	0/70 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Ibandronate	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	19/70 (27.14%)	26/70 (37.14%)
Gastrointestinal disorders		
Diarrhoea [A] *	3/70 (4.29%)	5/70 (7.14%)
Dyspepsia [A] *	0/70 (0%)	5/70 (7.14%)
Nausea [A] *	2/70 (2.86%)	4/70 (5.71%)
Infections and infestations		
Influenza [A] *	4/70 (5.71%)	2/70 (2.86%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	8/70 (11.43%)	4/70 (5.71%)
Back pain [A] *	4/70 (5.71%)	4/70 (5.71%)
Rheumatoid arthritis [A] *	4/70 (5.71%)	3/70 (4.29%)
Nervous system disorders		
Headache [A] *	2/70 (2.86%)	7/70 (10%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA

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 after the first publication or presentation that involves the overall study. Sponsor may request that confidential information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

Results Point of Contact:

Name/Official Title: Medical Communications
Organization: Hoffmannb-LaRoche
Phone: 800-821-8590
Email: genentech@druginfo.com