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ClinicalTrials.gov ID: NCT00542425

Study Identification

Unique Protocol ID: BA058-05-002

Brief Title: Phase 2 Dose-finding Study to Evaluate the Effects of BA058 in the Treatment of Postmenopausal Women With Osteoporosis

Official Title: A Randomized, Parallel-Group, Phase 2 Dose-finding Study to Evaluate the Effects of BA058 in the Treatment of Postmenopausal Women With Osteoporosis

Study Status

Record Verification: September 2017

Overall Status: Completed

Study Start: April 2007

Primary Completion: June 2009 [Actual]

Study Completion: June 2009 [Actual]

Sponsor/Collaborators

Sponsor: Radius Health, Inc.

Responsible Party: Sponsor

Study Description

Brief Summary: The purpose of this study is to determine whether BA058 is effective in building bone in postmenopausal women with osteoporosis.

Detailed Description: This is a randomized, parallel-group, multi-center, dose-finding study to evaluate the effects of BA058 in the treatment of otherwise healthy postmenopausal women with osteoporosis.

Conditions

Conditions: Osteoporosis

Keywords: osteoporosis
postmenopausal
bone loss

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 2

Interventional Study Model: Parallel Assignment

Number of Arms: 5

Masking: Triple (Participant, Care Provider, Investigator)

Allocation: Randomized

Enrollment: 222 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo Placebo subcutaneous daily
Experimental: BA058 20 µg	Drug: BA058 20 µg BA058 20 µg subcutaneous daily
Experimental: BA058 40 µg	Drug: BA058 40 µg BA058 40 µg subcutaneous daily
Experimental: BA058 80 µg	Drug: BA058 80 µg BA058 80 µg subcutaneous daily
Active Comparator: teriparatide	Drug: teriparatide teriparatide 20 µg subcutaneous daily Other Names: • PTH

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 55 Years

Maximum Age: 85 Years

Sex: Female

Gender Based:

Accepts Healthy Volunteers: No

Criteria: Primary Inclusion Criteria:

- The patient has a bone mineral density T-score ≤ 2.5 at the lumbar spine or hip (femoral neck) by dual energy x-ray absorptiometry (DXA). Women with a bone mineral density T-score of 2.0 or lower and a prior low-trauma forearm, humerus, vertebral, sacral, pelvic, hip, femoral, or tibial fracture within the past 5 years, or who have an additional risk factor such as age 65 or greater or a strong maternal history of osteoporosis defined as a fracture related to osteoporosis or osteoporosis itself as determined by BMD criteria, are also study candidates.
- The patient is in good general health as determined by medical history and physical examination and is without evidence of clinically significant abnormality in the opinion of the Investigator.

Primary Exclusion Criteria:

- History of bone disorders (e.g., Paget's disease) other than postmenopausal osteoporosis.
- Prior treatment with approved or as yet unapproved bone-acting investigational agents.
- History of carcinoma, nephrolithiasis or urolithiasis within the past five years or osteosarcoma at any time.
- History of radiotherapy (radiation therapy).

Contacts/Locations

Central Contact Person: Clinical Operations
Telephone: 617 551-4700
Email: info@radiuspharm.com

Study Officials: Medical Director
Study Director
Radius Health, Inc.

Locations: **United States, Massachusetts**
Radius Health, Inc.
Cambridge, Massachusetts, United States, 02139

Study Results

Participant Flow

Recruitment Details	Recruitment for the study started in the US, in January 2007. For the initial 24-week treatment period, patients were randomized to study treatment at 30 study centers in the US, Argentina, India and the UK . Eleven of the 30 study centers treated patients in the 24-week treatment extension period in the US, Argentina, and India.
Pre-assignment Details	After eligibility was established, patients entered a 4-week Pretreatment Period during which they received daily Calcium and Vitamin D supplements, were trained in self-injection with the pen devices, and were assessed for additional evaluations at the end of the Pretreatment Period. Patients who remained eligible were randomized on Day 1.

Reporting Groups

	Description
Placebo	[Not Specified]
BA058 20 µg	[Not Specified]
BA058 40 µg	[Not Specified]
BA058 80 µg	[Not Specified]
Teriparatide	[Not Specified]

Initial 24 Weeks

	Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide
Started	46	43	43	45	45
Completed	42	33	36	34	39
Not Completed	4	10	7	11	6
Administrative reasons	0	0	1	1	0
Adverse Event	0	1	1	3	2
Inability to complete procedures	0	3	2	1	2
Lost to Follow-up	2	2	1	0	0

	Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide
Non-compliance	0	0	0	1	1
Protocol Violation	0	0	0	1	0
Refusal of treatment	2	2	1	4	1
Other	0	2	1	0	0

Extended 24 Weeks of Treatment

	Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide
Started	11 [1]	13 [1]	10 [1]	7 [1]	14 [1]
Completed	10	11	8	6	13
Not Completed	1	2	2	1	1
Adverse Event	0	0	1	1	0
Protocol Violation	0	0	1	0	0
Refusal of treatment	0	1	0	0	0
Other	1	1	0	0	1

[1] Not all patients were eligible for extension study, often due to the regulatory approval timeline.

Baseline Characteristics

Reporting Groups

	Description
Placebo	[Not Specified]
BA058 20 µg	[Not Specified]
BA058 40 µg	[Not Specified]
BA058 80 µg	[Not Specified]
Teriparatide	[Not Specified]

Baseline Measures

		Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide	Total
Overall Number of Participants		46	43	43	45	45	222
Age, Continuous	Number Analyzed	46 participants	43 participants	43 participants	45 participants	45 participants	222 participants
	Mean (Standard Deviation) Unit of measure: years	65 (7.11)	66.3 (6.96)	64.5 (7.35)	64.8 (7.21)	64.5 (7.48)	65 (7.19)
Sex: Female, Male	Number Analyzed Measure Type: Count of Participants Unit of measure: participants	46 participants	43 participants	43 participants	45 participants	45 participants	222 participants
	Female	46 100%	43 100%	43 100%	45 100%	45 100%	222 100%
	Male	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change in Marker of Bone Metabolism, PINP
Measure Description	PINP, N-terminal propeptide of type I procollagen, is a marker of anabolic bone growth.
Time Frame	6 months

Analysis Population Description

The intent to treat (ITT) population included any patient who received at least one dose of study medication; N=221. 193 of the 221 ITT patients had data available for analysis at Week 24.

Reporting Groups

	Description
Placebo	[Not Specified]
BA058 20 µg	[Not Specified]
BA058 40 µg	[Not Specified]
BA058 80 µg	[Not Specified]
Teriparatide	[Not Specified]

Measured Values

	Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide
Overall Number of Participants Analyzed	38	34	37	42	42
Change in Marker of Bone Metabolism, PINP Mean (Standard Deviation) Unit of measure: Percent change from baseline	-13.1 (26.47)	20.0 (61.05)	90.8 (116.92)	97.2 (123.88)	154.3 (213.07)

Statistical Analysis 1 for Change in Marker of Bone Metabolism, PINP

Statistical Analysis Overview	Comparison Group Selection	Placebo, BA058 40 µg
	Comments	Study size provided 95 percent power to detect a difference in means of 114 (ng/mL) for PINP endpoint between BA058 (SD=147.5) and placebo (SD=34.5). Study size was based on Bauer 2006 data and utilized a 2-tailed 2-sample t-test with a significance level of alpha=0.01 with a Bonferonni adjustment for multiple testing. It included a 10 percent adjustment for within study dropouts over 6 months and a 15 percent adjustment to maintain adequate power for a per protocol analysis of key endpoints.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

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

Statistical Analysis 2 for Change in Marker of Bone Metabolism, PINP

Statistical Analysis Overview	Comparison Group Selection	Placebo, BA058 80 µg
	Comments	Study size provided 95 percent power to detect a difference in means of 114 (ng/mL) for PINP endpoint between BA058 (SD=147.5) and placebo (SD=34.5). Study size was based on Bauer 2006 data and utilized a 2-tailed 2-sample t-test with a significance level of alpha=0.01 with a Bonferonni adjustment for multiple testing. It included a 10 percent adjustment for within study dropouts over 6 months and a 15 percent adjustment to maintain adequate power for a per protocol analysis of key endpoints.

	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

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

2. Primary Outcome Measure:

Measure Title	Change in Bone Mineral Density, Total Spine.
Measure Description	Total analyzable spine bone mineral density (BMD) was analyzed by DXA at Week 24.
Time Frame	6 months

Analysis Population Description

The intent to treat (ITT) population included any patient who received at least one dose of study medication; N=221. 187 of the 221 ITT patients had data available for analysis at Week 24.

Reporting Groups

	Description
Placebo	[Not Specified]
BA058 20 µg	[Not Specified]
BA058 40 µg	[Not Specified]
BA058 80 µg	[Not Specified]
Teriparatide	[Not Specified]

Measured Values

	Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide
Overall Number of Participants Analyzed	42	32	37	36	40
Change in Bone Mineral Density, Total Spine. Mean (Standard Deviation) Unit of measure: Percent change from baseline	1.22 (3.211)	3.30 (2.068)	5.21 (4.427)	6.11 (3.744)	5.47 (4.218)

Statistical Analysis 1 for Change in Bone Mineral Density, Total Spine.

Statistical Analysis Overview	Comparison Group Selection	Placebo, BA058 40 µg
	Comments	For the BMD endpoint, the planned study size has 80 percent power with alpha=0.02 to detect a difference in mean change from baseline of 3.0 (percent) in BMD for the BA058 group and the BA058 Placebo group using an assumed SD of 3.5-4.0. The estimates for SD are based upon results of lumbar spine BMD presented by Body 2002.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

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

Statistical Analysis 2 for Change in Bone Mineral Density, Total Spine.

Statistical Analysis Overview	Comparison Group Selection	Placebo, BA058 80 µg
	Comments	For the BMD endpoint, the planned study size has 80 percent power with alpha=0.02 to detect a difference in mean change from baseline of 3.0 (percent) in BMD for the BA058 group and the BA058 Placebo group using an assumed SD of 3.5-4.0. The estimates for SD are based upon results of lumbar spine BMD presented by Body 2002.
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

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

3. Secondary Outcome Measure:

Measure Title	Change in Bone Mineral Density, Femoral Neck.
Measure Description	Femoral neck bone mineral density (BMD) was analyzed by DXA at Week 24.
Time Frame	6 months

Analysis Population Description

The intent to treat (ITT) population included any patient who received at least one dose of study medication; N=221. 182 of the 221 ITT patients had data available for analysis at Week 24.

Reporting Groups

	Description
Placebo	[Not Specified]
BA058 20 µg	[Not Specified]
BA058 40 µg	[Not Specified]
BA058 80 µg	[Not Specified]
Teriparatide	[Not Specified]

Measured Values

	Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide
Overall Number of Participants Analyzed	41	31	37	35	38
Change in Bone Mineral Density, Femoral Neck. Mean (Standard Deviation) Unit of measure: Percent change from baseline	0.79 (4.797)	2.69 (4.022)	2.20 (4.406)	3.07 (4.175)	1.07 (4.564)

4. Secondary Outcome Measure:

Measure Title	Change in Bone Mineral Density, Total Hip.
Measure Description	Total analyzable hip bone mineral density (BMD) was analyzed by DXA at Week 24.
Time Frame	6 months

Analysis Population Description

The intent to treat (ITT) population included any patient who received at least one dose of study medication; N=221. 182 of the 221 ITT patients had data available for analysis at Week 24.

Reporting Groups

	Description
Placebo	[Not Specified]
BA058 20 µg	[Not Specified]
BA058 40 µg	[Not Specified]
BA058 80 µg	[Not Specified]
Teriparatide	[Not Specified]

Measured Values

	Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide
Overall Number of Participants Analyzed	41	31	37	35	38
Change in Bone Mineral Density, Total Hip. Mean (Standard Deviation) Unit of measure: Percent change from baseline	0.39 (3.053)	1.43 (2.639)	1.97 (3.699)	2.60 (3.488)	0.45 (3.925)

5. Secondary Outcome Measure:

Measure Title	Change in Bone Mineral Density, Total Spine.
Measure Description	Total analyzable spine bone mineral density (BMD) was analyzed by DXA at Week 48.
Time Frame	12 months

Analysis Population Description

The extension population included any patient who continued in the extended 24 weeks of treatment; N=55. 49 of the 55 extension patients had data available for analysis at Week 48.

Reporting Groups

	Description
Placebo	[Not Specified]
BA058 20 µg	[Not Specified]
BA058 40 µg	[Not Specified]
BA058 80 µg	[Not Specified]
Teriparatide	[Not Specified]

Measured Values

	Placebo	BA058 20 µg	BA058 40 µg	BA058 80 µg	Teriparatide
Overall Number of Participants Analyzed	10	11	9	6	13
Change in Bone Mineral Density, Total Spine.	Mean (Standard Deviation) 0.74 (3.541) Unit of measure: Percent change from baseline	5.14 (3.164)	9.84 (5.313)	12.94 (3.251)	8.63 (6.8)

Reported Adverse Events

Time Frame	For patients treated during the initial 6 months only, AEs were collected for 8 months (1 pre + 6 treatment + 1 post). For patients treated over the extended treatment period of 12 months, AEs were collected for 14 months (1 pre + 12 treatment + 1 post).
Adverse Event Reporting Description	Method of routinely determining whether or not certain adverse events have occurred was by regular investigator assessment and regular laboratory testing.

Reporting Groups

	Description
Placebo	[Not Specified]
BA058 20 µg	[Not Specified]
BA058 40 µg	[Not Specified]
BA058 80 µg	[Not Specified]
Teriparatide	[Not Specified]

Serious Adverse Events

	Placebo		BA058 20 µg		BA058 40 µg		BA058 80 µg		Teriparatide	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	1/45 (2.22%)		2/43 (4.65%)		0/43 (0%)		2/45 (4.44%)		0/45 (0%)	
Gastrointestinal disorders										
Ascites [A] †	0/45 (0%)	0	1/43 (2.33%)	1	0/43 (0%)	0	0/45 (0%)	0	0/45 (0%)	0
Infections and infestations										
Bronchitis [A] †	1/45 (2.22%)	1	0/43 (0%)	0	0/43 (0%)	0	0/45 (0%)	0	0/45 (0%)	0
Diverticulitis [A] †	0/45 (0%)	0	0/43 (0%)	0	0/43 (0%)	0	1/45 (2.22%)	1	0/45 (0%)	0
Musculoskeletal and connective tissue disorders										
Bilateral crural hernia [A] †	0/45 (0%)	0	0/43 (0%)	0	0/43 (0%)	0	1/45 (2.22%)	1	0/45 (0%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)										
Ovarian epithelial cancer [A] †	0/45 (0%)	0	1/43 (2.33%)	1	0/43 (0%)	0	0/45 (0%)	0	0/45 (0%)	0

†Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (11.1)

Other Adverse Events

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

	Placebo		BA058 20 µg		BA058 40 µg		BA058 80 µg		Teriparatide	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	30/45 (66.67%)		31/43 (72.09%)		32/43 (74.42%)		33/45 (73.33%)		35/45 (77.78%)	
Cardiac disorders										
Palpitations [A] †	0/45 (0%)		0/43 (0%)		0/43 (0%)		3/45 (6.67%)		1/45 (2.22%)	
Gastrointestinal disorders										
Abdominal pain [A] †	1/45 (2.22%)		3/43 (6.98%)		1/43 (2.33%)		0/45 (0%)		0/45 (0%)	
Diarrhea [A] †	0/45 (0%)		1/43 (2.33%)		5/43 (11.63%)		3/45 (6.67%)		3/45 (6.67%)	
Nausea [A] †	0/45 (0%)		0/43 (0%)		5/43 (11.63%)		2/45 (4.44%)		2/45 (4.44%)	
Vomiting [A] †	0/45 (0%)		3/43 (6.98%)		2/43 (4.65%)		1/45 (2.22%)		1/45 (2.22%)	

	Placebo		BA058 20 µg		BA058 40 µg		BA058 80 µg		Teriparatide	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
General disorders										
Injection site hematoma [A] †	5/45 (11.11%)		2/43 (4.65%)		5/43 (11.63%)		1/45 (2.22%)		6/45 (13.33%)	
Injection site hemorrhage [A] †	0/45 (0%)		0/43 (0%)		0/43 (0%)		1/45 (2.22%)		3/45 (6.67%)	
Infections and infestations										
Bronchitis [A] †	1/45 (2.22%)		3/43 (6.98%)		2/43 (4.65%)		3/45 (6.67%)		2/45 (4.44%)	
Gastroenteritis [A] †	0/45 (0%)		1/43 (2.33%)		2/43 (4.65%)		3/45 (6.67%)		0/45 (0%)	
Influenza [A] †	7/45 (15.56%)		1/43 (2.33%)		3/43 (6.98%)		5/45 (11.11%)		6/45 (13.33%)	
Nasopharyngitis [A] †	2/45 (4.44%)		5/43 (11.63%)		2/43 (4.65%)		3/45 (6.67%)		6/45 (13.33%)	
Upper respiratory tract infection [A] †	0/45 (0%)		2/43 (4.65%)		1/43 (2.33%)		0/45 (0%)		3/45 (6.67%)	
Urinary tract infection [A] †	1/45 (2.22%)		4/43 (9.3%)		1/43 (2.33%)		1/45 (2.22%)		4/45 (8.89%)	
Metabolism and nutrition disorders										
Hypercalcemia [A] †	1/45 (2.22%)		1/43 (2.33%)		3/43 (6.98%)		2/45 (4.44%)		4/45 (8.89%)	
Hypertriglyceridemia [A] †	0/45 (0%)		4/43 (9.3%)		0/43 (0%)		0/45 (0%)		1/45 (2.22%)	
Musculoskeletal and connective tissue disorders										
Arthralgia [A] †	4/45 (8.89%)		2/43 (4.65%)		5/43 (11.63%)		1/45 (2.22%)		3/45 (6.67%)	
Back pain [A] †	5/45 (11.11%)		3/43 (6.98%)		6/43 (13.95%)		0/45 (0%)		1/45 (2.22%)	
Nervous system disorders										
Headache [A] †	3/45 (6.67%)		2/43 (4.65%)		6/43 (13.95%)		6/45 (13.33%)		6/45 (13.33%)	
Sciatica [A] †	0/45 (0%)		0/43 (0%)		3/43 (6.98%)		1/45 (2.22%)		0/45 (0%)	
Renal and urinary disorders										
Hypercalciuria [A] †	4/45 (8.89%)		3/43 (6.98%)		2/43 (4.65%)		4/45 (8.89%)		4/45 (8.89%)	
Respiratory, thoracic and mediastinal disorders										
Cough [A] †	0/45 (0%)		2/43 (4.65%)		3/43 (6.98%)		2/45 (4.44%)		0/45 (0%)	

†Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (11.1)

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 PI/Institution may publish/present results of the Study provided that the Publication is reviewed by the Sponsor for Confidential Information at least 60 days prior to submission. If the Publication contains patent-related information, the submission shall be delayed for 90 days.

The Institution/PI will not publish until after the data from the multi-center study is published in a combined paper as long as it is completed within 18 months from the date of study completion.

Results Point of Contact:

Name/Official Title: Program Director
Organization: Radius Health, Inc.
Phone: (617) 551-4700
Email: info@radiuspharm.com