ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 08/01/2013

ClinicalTrials.gov ID: NCT00933686

Study Identification

Unique Protocol ID:	27560
Brief Title:	Growth Hormone in Neuroendocrine Dysfunction With Severe Fibromyalgia Syndrome
Official Title:	Growth Hormone Treatment of Severe Fibromyalgia Syndrome Associated With Functional Failure of Somatotropic Axis. A Multicentre, Randomized, Double-blind, Placebo-controlled Study.
Secondary IDs:	

Study Status

Record Verification:	August 2013
Overall Status:	Completed
Study Start:	December 2007
Primary Completion:	July 2010 [Actual]
Study Completion:	July 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Merck KGaA
Responsible Party:	Sponsor
Collaborators:	Merck, S.L., Spain

Oversight

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

Review Board:	Approval Status: Approved Approval Number: 01/15/2007 Board Name: Comité Ético de Investigación Clínica Board Affiliation: Comité Etico de Investigación Clínica del Centro Médico Teknon Phone: +34 93 290 62 68 Email: ceic@cmteknon.com
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Spain: Spanish Agency of Medicines

Study Description

Brief Summary:	The purpose of this study is to evaluate the efficacy of recombinant human growth hormone (r-hGH) treatment in severe fibromyalgia subjects with growth axis dysfunction.
Detailed Description:	

Conditions

Conditions:	Fibromyalgia
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Crossover Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	113 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: Saizen®	Drug: Saizen® Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) will be administered subcutaneously daily for 12 months. Dose will be titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) is less than 50 percent of the baseline value. Dose titrations will be made at Month 1, 3, 7 and 9. Other Names: • Somatropin
Active Comparator: Placebo + Saizen®	Drug: Placebo and Saizen® Placebo matched to Saizen® will be administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose will be titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) is less than 50 percent of the baseline value. Dose titrations will be made at Month 7 and 9.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Female

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Women aged greater than or equal (>=) 18 years
- Fibromyalgia diagnosed at least one year before
- History of generalized pain and at least 16 positive tender points (1990 American College of Rheumatology [ACR] criteria)
- Body Mass Index (BMI) less than or equal to(=<) 32
- Normal GH stimulation test (insulin)
- Stable (>= 3 months unchanged) standard treatment with amitriptyline (10-50 milligram per day [mg/day]) plus selective serotonin reuptake inhibitor (10-40 mg/day) plus tramadol (25-400 mg/day)
- Active rehabilitation program during the previous year (at least 30 minutes/day)
- Fibromyalgia Impact Questionnaire (FIQ) score >=75

- IGF-1 serum level =< 150 nanogram/milliliter (ng/mL) otherwise =< 2 SD of the local lab normality)
- Normal response to IGF-1 generation test
- Chronic Fatigue Symptoms (Multidimensional Assessment of Fatigue [MAF])
- Effective anti-conception
- Willingness to comply with the protocol
- Written Informed consent

Exclusion Criteria:

- Major psychiatric condition
- Rheumatic disease, including systemic lupus erythematosus (SLE)
- Previous or current malignancies, active or inactive
- Clinical history intracranial space occupying lesion
- Reactive or secondary (rheumatoid arthritis [RA], osteoarthritis) fibromyalgia syndrome (FMS)
- Antinuclear antibody (ANA) greater than or equal 1:80
- Abnormal Creatine phosphokinase (CPK) or aldolase serum levels
- Not controlled thyroid disease in the last 3 months (free Thyroxine [T4] and Thyrotrophin-stimulating hormone [TSH] serum levels)
- Diabetes mellitus
- Adrenal gland disease (any abnormal cortisolemia, will be confirmed by 24-hour cortisoluria)
- Pregnancy or breast feeding
- Known to be hypersensitive to somatotropin or any of the excipients

Contacts/Locations

Study Officials: Guillem Cuatrecasas, MD
Study Principal Investigator
Centro Medico Teknon

Locations: Spain
Centro Medico Teknon, Endocrinology Department
Barcelona, Spain

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Recruitment Details	123 subjects were enrolled of whom 113 subjects were randomised and treated.

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Overall Study

	Saizen®	Placebo + Saizen®
Started	55	58
Completed	45	47
Not Completed	10	11
Protocol Violation	0	1
Lost to Follow-up	2	2
Withdrawal by Subject	6	5
Adverse Event	1	1
Physician Decision	1	0
Failure to show up at endpoint visits	0	2

Baseline Characteristics

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Baseline Measures

	Saizen®	Placebo + Saizen®	Total
Number of Participants	55	58	113
Age, Continuous [units: years] Mean (Standard Deviation)	49.9 (9.5)	50.3 (9.6)	50.1 (9.5)
Gender, Male/Female [units: participants]			
Female	55	58	113
Male	0	0	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Less Than 11 Tender Points at Month 6
Measure Description	The musculoskeletal component in form of pain on palpation in at least 11 of 18 tender point sites is required to fulfill the American College of Rheumatology (ACR) criteria for fibromyalgia syndrome, An important response is considered when the number of tender points falls below 11 since it is the threshold for fibromyalgia diagnosis.
Time Frame	Month 6
Safety Issue?	No

Analysis Population Description

Intention-to-treat (ITT) population included all the participants who were randomized in the study. 'N' signifies number of participants who were evaluable for this outcome measure.

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Measured Values

	Saizen®	Placebo + Saizen®
Number of Participants Analyzed	51	50
Percentage of Participants With Less Than 11 Tender Points at Month 6 [units: Percentage of participants]	20	22

2. Primary Outcome Measure:

Measure Title	Percentage of Participants With Less Than 11 Tender Points at Month 12
Measure Description	The musculoskeletal component in form of pain on palpation in at least 11 of 18 tender point sites is required to fulfill the ACR criteria for fibromyalgia syndrome, An important response is considered when the number of tender points falls below 11 since it is the threshold for fibromyalgia diagnosis.
Time Frame	Month 12
Safety Issue?	No

Analysis Population Description

ITT population included all the participants who were randomized in the study. 'N' signifies number of participants who were evaluable for this outcome measure.

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Measured Values

	Saizen®	Placebo + Saizen®
Number of Participants Analyzed	45	47
Percentage of Participants With Less Than 11 Tender Points at Month 12 [units: Percentage of participants]	53	34

3. Secondary Outcome Measure:

Measure Title	Fibromyalgia Impact Questionnaire (FIQ) Total Score
Measure Description	Fibromyalgia Impact Questionnaire (FIQ) is a 10-item questionnaire that measures physical impairment, well-being, missed work, pain, fatigue, rest, stiffness, anxiety, and depression. Score ranges from 0 (best result - very well) to 100 (worst result - awful).
Time Frame	Baseline, Month 1, 3, 6, 7, 9 and 12
Safety Issue?	No

Analysis Population Description

ITT population included all the participants who were randomized in the study. 'N' signifies number of participants who were evaluable for this outcome measure. 'n' signifies number of participants who were evaluable at each time-point for each arm group.

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.

	Description
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Measured Values

	Saizen®	Placebo + Saizen®
Number of Participants Analyzed	54	57
Fibromyalgia Impact Questionnaire (FIQ) Total Score [units: Units on a scale] Mean (Standard Deviation)		
Baseline (n=54, 57)	85.7 (2.3)	86.0 (1.8)
Month 1 (n=52, 54)	74.6 (3.6)	73.3 (4.7)
Month 3 (n=52, 54)	72.1 (4.4)	66.4 (5.1)
Month 6 (n=51, 50)	65.8 (4.8)	68.4 (5.3)
Month 7 (n=51, 50)	59.2 (5.5)	65.8 (5.7)
Month 9 (n=51, 50)	58.2 (6.4)	65.1 (5.7)
Month 12 (n=45, 47)	52.5 (6.5)	64.7 (6.5)

4. Secondary Outcome Measure:

Measure Title	Visual Analog Scale (VAS) Total Score
Measure Description	Visual Analog Scale (VAS) is a 100 millimeter (mm) scale. Intensity of pain range: 0 mm=no pain to 100 mm=worst possible pain.
Time Frame	Baseline, Month 1, 3, 6, 7, 9 and 12
Safety Issue?	No

Analysis Population Description

ITT population included all the participants who were randomized in the study. 'N' signifies number of participants who were evaluable for this outcome measure. 'n' signifies number of participants who were evaluable at each time-point for each arm group.

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Measured Values

	Saizen®	Placebo + Saizen®
Number of Participants Analyzed	54	57
Visual Analog Scale (VAS) Total Score [units: mm] Mean (Standard Deviation)		
Baseline (n=54, 57)	73.3 (3.4)	74.3 (3.1)
Month 1 (n=52, 54)	65.1 (4.2)	68.0 (5.7)
Month 3 (n=52, 54)	63.7 (5.6)	58.4 (5.8)
Month 6 (n=51, 50)	57.6 (5.7)	60.4 (6.6)
Month 7 (n=51, 50)	54.6 (5.2)	56.1 (6.2)
Month 9 (n=51, 50)	51.2 (6.7)	60.3 (6.3)
Month 12 (n=45, 47)	45.0 (6.9)	60.6 (6.0)

5. Secondary Outcome Measure:

Measure Title	EuroQol 5-Dimensions (EQ-5D) Total Score
Measure Description	EuroQol 5-Dimensions (EQ-5D) questionnaire is a measure of health status and quality of life (QoL). The EQ-5D defines health in terms of mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Score range for each item is 0 to 3, with 3 being the most severe. Total score range is 0 to 15. Lower scores represent a better QoL.
Time Frame	Baseline, Month 1, 3, 6, 7, 9 and 12
Safety Issue?	No

Analysis Population Description

ITT population included all the participants who were randomized in the study. 'N' signifies number of participants who were evaluable for this outcome measure. 'n' signifies number of participants who were evaluable at each time-point for each arm group.

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Measured Values

	Saizen®	Placebo + Saizen®
Number of Participants Analyzed	54	57
EuroQol 5-Dimensions (EQ-5D) Total Score [units: Units on a scale] Mean (Standard Deviation)		
Baseline (n=54, 57)	11.07 (0.44)	11.24 (0.42)
Month 1 (n=52, 54)	10.46 (0.45)	10.45 (0.42)
Month 3 (n=52, 54)	10.13 (0.45)	10.06 (0.55)
Month 6 (n=51, 50)	10.00 (0.48)	10.16 (0.56)
Month 7 (n=51, 50)	9.63 (0.49)	9.77 (0.54)
Month 9 (n=51, 50)	9.49 (0.60)	9.80 (0.50)
Month 12 (n=45, 47)	9.09 (0.64)	9.94 (0.56)

6. Secondary Outcome Measure:

Measure Title	Multidimensional Assessment of Fatigue (MAF) Total Score

Measure Description	Multidimensional Assessment of Fatigue (MAF) consists of 16 questions. The score range for first 14 questions is between 0 and 10 for each question while for the last two questions it is 0 and 4 for each question. Total score range for first 14 questions is 0 to 100 and for last two questions is 0 to 8. Lower scores on the each represent the better participant's condition, whereas, higher scores indicate worsening condition.
Time Frame	Baseline, Month 6 and 12
Safety Issue?	No

Analysis Population Description

ITT population included all the participants who were randomized in the study. 'N' signifies number of participants who were evaluable for this outcome measure. 'n' signifies number of participants who were evaluable at each time-point for each arm group.

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Measured Values

	Saizen®	Placebo + Saizen®
Number of Participants Analyzed	54	57
Multidimensional Assessment of Fatigue (MAF) Total Score [units: Units on a scale]		
1 to 14 questions: Baseline (n=54, 57)	90	83
1 to 14 questions: Month 6 (n=51, 50)	85	78
1 to 14 questions: Month 12 (n=45, 47)	73	78
15 and 16 question: Baseline (n=54, 57)	7	7
15 and 16 question: Month 6 (n=51, 50)	6	6
15 and 16 question: Month 12 (n=45, 47)	5	6

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Positive Response on Quality of Life Assessment of Growth Hormone [GH] Deficiency in Adults (QoL AGHDA) Scale
Measure Description	Quality of Life Assessment of GH Deficiency in Adults (QoL AGHDA) questionnaire consists of 25 items that evoke yes or no answers. A score of 1 is given to each item affirmed and these are summed to give the total score. The maximum score is 25, which represents a poor quality of life. The minimum score is 0, which represents a good quality of life. Each question has to be answered with a NO/YES and for each YES, one point is added. The more YES, the higher the score and the worse. Decrease in the positive responses is an index of improvement. So, when the percentage of positive responses on the scale decreases, it is considered a response rate.
Time Frame	Baseline, Month 6 and 12
Safety Issue?	No

Analysis Population Description

ITT population included all the participants who were randomized in the study. 'N' signifies number of participants who were evaluable for this outcome measure. 'n' signifies number of participants who were evaluable at each time-point for each arm group.

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Measured Values

	Saizen®	Placebo + Saizen®
Number of Participants Analyzed	54	57
Percentage of Participants With Positive Response on Quality of Life Assessment of Growth Hormone [GH] Deficiency in Adults (QoL AGHDA) Scale [units: Percentage of participants]		
Baseline (n=54, 57)	73	72
Month 6 (n=51, 50)	70	69
Month 12 (n=45, 47)	59	70

Reported Adverse Events

Time Frame	Baseline up to Month 12
Additional Description	[Not specified]

Reporting Groups

	Description
Saizen®	Saizen® (Somatropin) 0.006 milligram per kilogram (mg/kg) was administered subcutaneously daily for 12 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in insulin-like growth factor 1 (IGF-1) was less than 50 percent of the baseline value. Dose titrations were made at Month 1, 3, 7 and 9.
Placebo + Saizen®	Placebo matched to Saizen® was administered for the first 6 months followed by treatment with Saizen® (Somatropin) 0.006 mg/kg subcutaneously daily for next 6 months. Saizen® dose was titrated (an increase of 0.2 milligram per day) if the increase in IGF-1 was less than 50 percent of the baseline value. Dose titrations were made at Month 7 and 9.

Serious Adverse Events

	Saizen®	Placebo + Saizen®
	Affected/At Risk (%)	Affected/At Risk (%)
Total	4/55 (7.27%)	0/58 (0%)
Gastrointestinal disorders		
Abdominal pain lower [A] *	1/55 (1.82%)	0/58 (0%)
Immune system disorders		
Food allergy [A] *	1/55 (1.82%)	0/58 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Cervix carcinoma [A] *	1/55 (1.82%)	0/58 (0%)
Nervous system disorders		
Sleep apnoea syndrome [A] *	1/55 (1.82%)	0/58 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (Unspecified)

Other Adverse Events

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

	Saizen®	Placebo + Saizen®
	Affected/At Risk (%)	Affected/At Risk (%)
Total	45/55 (81.82%)	51/58 (87.93%)
Blood and lymphatic system disorders		
Anaemia [A] *	1/55 (1.82%)	0/58 (0%)
Iron deficiency anaemia [A] *	0/55 (0%)	2/58 (3.45%)
Microcytic anaemia [A] *	0/55 (0%)	1/58 (1.72%)
Cardiac disorders		
Tachycardia [A] *	0/55 (0%)	8/58 (13.79%)
Ear and labyrinth disorders		
Dizziness [A] *	0/55 (0%)	5/58 (8.62%)
Ear infection [A] *	0/55 (0%)	1/58 (1.72%)
Otitis media acute [A] *	1/55 (1.82%)	0/58 (0%)
Endocrine disorders		
Hypothyroidism [A] *	0/55 (0%)	2/58 (3.45%)
Eye disorders		
Vision blurred [A] *	1/55 (1.82%)	0/58 (0%)
Visual acuity reduced [A] *	1/55 (1.82%)	0/58 (0%)
Gastrointestinal disorders		
Abdominal distension [A] *	4/55 (7.27%)	0/58 (0%)
Abdominal pain [A] *	3/55 (5.45%)	1/58 (1.72%)
Acetonaemic vomiting [A] *	0/55 (0%)	2/58 (3.45%)

	Saizen®	Placebo + Saizen®
	Affected/At Risk (%)	Affected/At Risk (%)
Aptyalism [A] *	1/55 (1.82%)	1/58 (1.72%)
Cheilitis [A] *	1/55 (1.82%)	0/58 (0%)
Constipation [A] *	0/55 (0%)	7/58 (12.07%)
Diarrhoea [A] *	0/55 (0%)	2/58 (3.45%)
Dysgeusia [A] *	0/55 (0%)	1/58 (1.72%)
Dyspepsia [A] *	0/55 (0%)	2/58 (3.45%)
Flatulence [A] *	1/55 (1.82%)	0/58 (0%)
Gastritis [A] *	0/55 (0%)	1/58 (1.72%)
Hiatus hernia [A] *	1/55 (1.82%)	0/58 (0%)
Nausea [A] *	5/55 (9.09%)	1/58 (1.72%)
Rectal haemorrhage [A] *	1/55 (1.82%)	0/58 (0%)
Toothache [A] *	0/55 (0%)	2/58 (3.45%)
Vomiting [A] *	1/55 (1.82%)	0/58 (0%)
General disorders		
Asthenia [A] *	1/55 (1.82%)	0/58 (0%)
Fall [A] *	0/55 (0%)	2/58 (3.45%)
Fatigue [A] *	0/55 (0%)	5/58 (8.62%)
Malaise [A] *	0/55 (0%)	1/58 (1.72%)
Pain [A] *	2/55 (3.64%)	0/58 (0%)
Pain exacerbated [A] *	5/55 (9.09%)	5/58 (8.62%)
Hepatobiliary disorders		
Transaminases increased [A] *	0/55 (0%)	1/58 (1.72%)

	Saizen®	Placebo + Saizen®
	Affected/At Risk (%)	Affected/At Risk (%)
Immune system disorders		
Food allergy [A] *	0/55 (0%)	1/58 (1.72%)
Hypersensitivity [A] *	1/55 (1.82%)	0/58 (0%)
Infections and infestations		
Corneal infection [A] *	0/55 (0%)	2/58 (3.45%)
Gastroenteritis [A] *	0/55 (0%)	3/58 (5.17%)
Localised infection [A] *	0/55 (0%)	1/58 (1.72%)
Vaginal candidiasis [A] *	4/55 (7.27%)	0/58 (0%)
Injury, poisoning and procedural complications		
Contusion [A] *	0/55 (0%)	3/58 (5.17%)
Injury asphyxiation [A] *	1/55 (1.82%)	1/58 (1.72%)
Ligament sprain [A] *	0/55 (0%)	2/58 (3.45%)
Tooth fracture [A] *	0/55 (0%)	1/58 (1.72%)
Investigations		
Arthroscopy [A] *	1/55 (1.82%)	0/58 (0%)
Blood pressure systolic increased [A] *	1/55 (1.82%)	0/58 (0%)
Metabolism and nutrition disorders		
Hypercholesterolaemia [A] *	3/55 (5.45%)	0/58 (0%)
Hyperglycaemia [A] *	1/55 (1.82%)	3/58 (5.17%)
Hypertriglyceridaemia [A] *	0/55 (0%)	8/58 (13.79%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	4/55 (7.27%)	8/58 (13.79%)
Arthritis [A] *	0/55 (0%)	1/58 (1.72%)

	Saizen®	Placebo + Saizen®
	Affected/At Risk (%)	Affected/At Risk (%)
Back pain [A] *	6/55 (10.91%)	0/58 (0%)
Bursitis [A] *	0/55 (0%)	3/58 (5.17%)
Epicondylitis [A] *	0/55 (0%)	1/58 (1.72%)
Fibromyalgia [A] *	1/55 (1.82%)	16/58 (27.59%)
Ganglion [A] *	0/55 (0%)	1/58 (1.72%)
Humerus fracture [A] *	1/55 (1.82%)	0/58 (0%)
Muscle contracture [A] *	0/55 (0%)	1/58 (1.72%)
Muscle cramp [A] *	0/55 (0%)	5/58 (8.62%)
Muscle rigidity [A] *	0/55 (0%)	5/58 (8.62%)
Muscle rupture [A] *	0/55 (0%)	1/58 (1.72%)
Musculoskeletal discomfort [A] *	0/55 (0%)	1/58 (1.72%)
Neck pain [A] *	4/55 (7.27%)	3/58 (5.17%)
Oedema [A] *	17/55 (30.91%)	15/58 (25.86%)
Osteitis [A] *	1/55 (1.82%)	0/58 (0%)
Pain in extremity [A] *	3/55 (5.45%)	5/58 (8.62%)
Pelvic fracture [A] *	1/55 (1.82%)	0/58 (0%)
Plantar fasciitis [A] *	0/55 (0%)	1/58 (1.72%)
Radius fracture [A] *	1/55 (1.82%)	0/58 (0%)
Synovitis [A] *	0/55 (0%)	1/58 (1.72%)
Tendonitis [A] *	0/55 (0%)	3/58 (5.17%)
Tenosynovitis [A] *	0/55 (0%)	1/58 (1.72%)
Trigger finger [A] *	3/55 (5.45%)	2/58 (3.45%)

	Saizen®	Placebo + Saizen®
	Affected/At Risk (%)	Affected/At Risk (%)
Wrist deformity [A] *	0/55 (0%)	1/58 (1.72%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adenoma benign [A] *	1/55 (1.82%)	0/58 (0%)
Ovarian cyst [A] *	1/55 (1.82%)	0/58 (0%)
Polyp colorectal [A] *	0/55 (0%)	1/58 (1.72%)
Nervous system disorders		
Carpal tunnel syndrome [A] *	8/55 (14.55%)	7/58 (12.07%)
Dysphemia [A] *	0/55 (0%)	1/58 (1.72%)
Headache [A] *	21/55 (38.18%)	13/58 (22.41%)
Insomnia [A] *	9/55 (16.36%)	2/58 (3.45%)
Migraine [A] *	0/55 (0%)	3/58 (5.17%)
Paraesthesia [A] *	13/55 (23.64%)	6/58 (10.34%)
Sciatica [A] *	2/55 (3.64%)	0/58 (0%)
Somnolence [A] *	2/55 (3.64%)	4/58 (6.9%)
Syncope [A] *	0/55 (0%)	6/58 (10.34%)
Tremor [A] *	0/55 (0%)	2/58 (3.45%)
Psychiatric disorders		
Amnesia [A] *	3/55 (5.45%)	0/58 (0%)
Anxiety [A] *	5/55 (9.09%)	0/58 (0%)
Depression [A] *	2/55 (3.64%)	1/58 (1.72%)
Memory impairment [A] *	0/55 (0%)	1/58 (1.72%)
Sleep talking [A] *	1/55 (1.82%)	0/58 (0%)
Renal and urinary disorders		

	Saizen®	Placebo + Saizen®
	Affected/At Risk (%)	Affected/At Risk (%)
Cystitis [A] *	3/55 (5.45%)	0/58 (0%)
Urinary incontinence [A] *	0/55 (0%)	1/58 (1.72%)
Urinary tract infection [A] *	7/55 (12.73%)	1/58 (1.72%)
Reproductive system and breast disorders		
Amenorrhoea [A] *	1/55 (1.82%)	0/58 (0%)
Breast pain [A] *	2/55 (3.64%)	0/58 (0%)
Hypertrophy breast [A] *	0/55 (0%)	2/58 (3.45%)
Menorrhagia [A] *	0/55 (0%)	4/58 (6.9%)
Respiratory, thoracic and mediastinal disorders		
Acute sinusitis [A] *	1/55 (1.82%)	0/58 (0%)
Bronchitis [A] *	0/55 (0%)	4/58 (6.9%)
Cough [A] *	0/55 (0%)	1/58 (1.72%)
Influenza [A] *	0/55 (0%)	1/58 (1.72%)
Laryngitis [A] *	0/55 (0%)	2/58 (3.45%)
Nasal congestion [A] *	0/55 (0%)	2/58 (3.45%)
Nasopharyngitis [A] *	0/55 (0%)	2/58 (3.45%)
Pharyngitis [A] *	2/55 (3.64%)	2/58 (3.45%)
Pneumonia [A] *	0/55 (0%)	1/58 (1.72%)
Rhinorrhoea [A] *	1/55 (1.82%)	0/58 (0%)
Sinusitis [A] *	1/55 (1.82%)	0/58 (0%)
Tonsillitis [A] *	0/55 (0%)	1/58 (1.72%)
Upper respiratory tract infection [A] *	6/55 (10.91%)	0/58 (0%)

	Saizen®	Placebo + Saizen®
	Affected/At Risk (%)	Affected/At Risk (%)
Skin and subcutaneous tissue disorders		
Alopecia [A] *	1/55 (1.82%)	0/58 (0%)
Erythema [A] *	0/55 (0%)	1/58 (1.72%)
Furuncle [A] *	0/55 (0%)	2/58 (3.45%)
Hyperhidrosis [A] *	3/55 (5.45%)	2/58 (3.45%)
Pruritus [A] *	0/55 (0%)	1/58 (1.72%)
Pruritus generalised [A] *	0/55 (0%)	1/58 (1.72%)
Social circumstances		
Impaired work ability [A] *	5/55 (9.09%)	7/58 (12.07%)
Wheelchair user [A] *	0/55 (0%)	1/58 (1.72%)
Vascular disorders		
Hot flush [A] *	1/55 (1.82%)	0/58 (0%)
Hypertension [A] *	4/55 (7.27%)	1/58 (1.72%)
Orthostatic hypotension [A] *	1/55 (1.82%)	0/58 (0%)

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

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.

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