ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 08/04/2013

ClinicalTrials.gov ID: NCT01237340

Study Identification

Unique Protocol ID:	EMR 701048-009
Brief Title:	Saizen® Solution for Injection Adult Growth Hormone Deficiency (GHD) Immunogenicity Study
Official Title:	A Phase IIIb, Open-label, Single-arm, Multicenter Study to Assess the Immunogenicity of the Recombinant-Human Growth Hormone (r-hGH) Liquid Multidose Formulation (Saizen® Solution for Injection) When Administered to Male and Female Adults With Documented Growth Hormone Deficiency (GHD)
Secondary IDs:	

Study Status

Record Verification:	August 2013
Overall Status:	Terminated
Study Start:	October 2010
Primary Completion:	December 2011 [Actual]
Study Completion:	December 2011 [Actual]

Sponsor/Collaborators

Sponsor:	EMD Serono
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 23,544 Serial Number: 097 Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 09/22/2010 Board Name: Schulman Associates Institutional Review Board, Inc. IRB # 1- biomedical; IRB # IRB00000971 Board Affiliation: Phone: 513.761.4100 Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration United States: Federal Government United States: Institutional Review Board Hungary: National Institute of Pharmacy Czech Republic: State Institute for Drug Control United Kingdom: Medicines and Healthcare Products Regulatory Agency

Study Description

Brief Summary:	To assess the immunogenicity of Saizen® solution for injection in adult subjects with documented Growth Hormone Deficiency (GHD).
Detailed Description:	

Conditions

Conditions:	Growth Hormone Deficiency (GHD)
Keywords:	Adult Growth Hormone Deficiency (AGHD) immunogenicity growth hormone antibodies GH biomarkers IGF-I

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	N/A
Endpoint Classification:	Safety Study
Enrollment:	59 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Saizen®	Drug: Saizen® Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling. Other Names: • r-hGH • Somatropin

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	60 Years
Gender:	Both
Accepts Healthy Volunteers?:	No

Criteria: Inclusion Criteria:

- Adult male and female subjects, 18-60 years of age, inclusive, at the time the informed consent is signed
- Subjects who have confirmed adult GHD
- Subjects who are growth hormone (GH) treatment-naive or had received Saizen® (freeze-dried formulation) for pediatric GHD (PGHD), or are currently receiving Saizen® freeze-dried formulation for adult GHD (AGHD)
- Subjects who have binding antibody-negative (BAbs-) at screening
- Subjects who have no evidence of concomitant disease, intercurrent illness, or resultant therapy that would interfere with subject compliance, the evaluation of study results, or compromise the safety of the subject
- Female subjects of childbearing potential who have a negative serum pregnancy test at the screening visit (and at each scheduled visit during the study)
- Subjects who are willing to comply with the procedures of the study
- Subjects who are willing to sign an Independent Ethics Committee/Institutional Review Board approved informed consent form
- Other protocol-defined inclusion criteria may apply

Exclusion Criteria:

- Subjects who are currently receiving or have previously received treatment for adult GHD or any other indication, including PGHD, with a commercial GH product other than Saizen® freeze-dried formulation
- Subjects who had a chronic underlying disease within 6 months prior to screening or concomitant medication(s) that in the opinion of the investigator would exclude the subject from the trial
- Subjects who have significant renal impairment
- Subjects who have diabetes mellitus
- Subjects who are immunosuppressed
- Subjects who have a current malignancy or a history of any malignancy (excluding fully-treated basal cell carcinoma)
- Subjects who have participated in another study and received an investigational drug within 30 days prior to screening visit
- Subjects who have clinically significant abnormal laboratory value(s)
- Subjects who have known hypersensitivity or allergy to exogenous human GH or any of the excipients or phenol, the bacteriostatic agent in the Saizen® solution for injection
- Other protocol-defined exclusion criteria may apply

Contacts/Locations

Study Officials: Medical Responsible
Study Director
Merck Serono S.A. - Geneva, an affiliate of Merck KGaA, Darmstadt, Germany

Locations: United States, Massachusetts
US Medical Information, Massachusetts, United States

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Saizen®	Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Overall Study

	Saizen®
Started	59
Completed	19
Not Completed	40
Adverse Event	3
Withdrawal by Subject	1
Early termination of the trial	36

Baseline Characteristics

Reporting Groups

	Description
Saizen®	Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Baseline Measures

	Saizen®
Number of Participants	59
Age, Continuous [units: years] Mean (Standard Deviation)	44.7 (10.3)
Gender, Male/Female [units: participants]	
Female	30
Male	29

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants Who Developed Positive Binding Antibodies (BAbs+) to Saizen®
Measure Description	Binding antibodies (BAbs) are all antibodies which are capable of binding to the investigational drug molecule (Saizen®), irrespective of their binding site.
Time Frame	Baseline up to Week 26
Safety Issue?	No

Analysis Population Description

Modified Intent-to-Treat (MITT) population consisted of all the participants who received at least 1 dose of study medication and had at least one post-baseline BAbs assessment.

Reporting Groups

	Description
Saizen®	Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Measured Values

	Saizen®
Number of Participants Analyzed	59
Number of Participants Who Developed Positive Binding Antibodies (BAbs+) to Saizen® [units: participants]	1

2. Secondary Outcome Measure:

Measure Title	Number of Participants Who Developed Positive Neutralizing Antibodies (NAbs+) to Saizen®
Measure Description	Neutralizing antibodies (NAbs) are defined as a subgroup of BAbs which bind to the active sites of the investigational drug molecule (Saizen®) and therefore neutralize its potency.
Time Frame	Baseline up to Week 26
Safety Issue?	No

Analysis Population Description

MITT population consisted of all the participants who received at least 1 dose of study medication and had at least one post-baseline BAbs assessment.

Reporting Groups

	Description
Saizen®	Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Measured Values

	Saizen®
Number of Participants Analyzed	59
Number of Participants Who Developed Positive Neutralizing Antibodies (NAbs+) to Saizen® [units: participants]	0

3. Secondary Outcome Measure:

Measure Title	Insulin-like Growth Factor-I (IGF-1) Levels
Measure Description	
Time Frame	Baseline, Week 2, Week 4, Week 8, Week 13, Week 18, Week 26
Safety Issue?	Yes

Analysis Population Description

Safety population consisted of all the participants who received at least 1 dose of study medication and had at least one post-baseline safety assessment. 'N' (number of participants analyzed) = participants who were evaluated for this measure and "n"= participants who were analyzed at that particular time point for each arm group respectively.

Reporting Groups

	Description
GH Treatment-Naive	Growth hormone (GH) Treatment-Naive participants were those who did not receive any prior treatment with Saizen® before initiation of the trial. Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.
GH Treatment-Experienced	Growth hormone (GH) Treatment-experienced participants were those who had undergone treatment with the freeze-dried formulation of Saizen® before initiation of the trial. Growth hormone (GH) Treatment-experienced participants were those who had undergone treatment with the freeze-dried formulation of Saizen® before initiation of the trial. Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Measured Values

	GH Treatment-Naive	GH Treatment-Experienced
Number of Participants Analyzed	49	8
Insulin-like Growth Factor-I (IGF-1) Levels [units: nanomole per liter (nmol/L)] Mean (Standard Deviation)		
Baseline (n = 49, 8)	11.492 (6.694)	20.225 (10.194)
Week 2 (n = 47, 8)	18.923 (10.394)	28.663 (9.001)
Week 4 (n = 49, 8)	19.914 (11.532)	24.500 (11.176)
Week 8 (n = 49, 8)	21.155 (10.520)	27.075 (6.815)
Week 13 (n = 46, 8)	23.415 (8.020)	26.413 (8.767)
Week 18 (n = 31, 4)	24.948 (9.300)	25.650 (8.502)
Week 26 (n = 48, 8)	24.117 (11.085)	27.438 (12.402)

4. Secondary Outcome Measure:

Measure Title	Insulin-like Growth Factor-I Standard Deviation Score (IGF-1 SDS)

Measure Description	Insulin-like Growth Factor-1 Standard Deviation Score (IGF-1 SDS) was provided by the central laboratory; its calculation is based on the actual value of IGF-1 minus mean reference value of IGF-1 divided by reference standard deviation of IGF-1.
Time Frame	Baseline, Week 2, Week 4, Week 8, Week 13, Week 18, Week 26
Safety Issue?	Yes

Analysis Population Description

Safety population consisted of all the participants who received at least 1 dose of study medication and had at least one post-baseline safety assessment. 'N' (number of participants analyzed) = participants who were evaluated for this measure and "n"= participants who were analyzed at that particular time point for each arm group respectively.

Reporting Groups

	Description
GH Treatment-Naive	Growth hormone (GH) Treatment-Naive participants were those who did not receive any prior treatment with Saizen® before initiation of the trial. Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.
GH Treatment-Experienced	Growth hormone (GH) Treatment-experienced participants were those who had undergone treatment with the freeze-dried formulation of Saizen® before initiation of the trial. Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Measured Values

	GH Treatment-Naive	GH Treatment-Experienced
Number of Participants Analyzed	49	8
Insulin-like Growth Factor-I Standard Deviation Score (IGF-1 SDS) [units: standard deviation score] Mean (Standard Deviation)		
Baseline (n = 49, 8)	-2.914 (2.268)	-0.550 (2.274)
Week 2 (n = 47, 8)	-0.926 (2.300)	0.951 (1.411)
Week 4 (n = 49, 8)	-0.867 (2.615)	0.153 (1.762)
Week 8 (n = 49, 8)	-0.464 (2.274)	0.834 (1.063)
Week 13 (n = 46, 8)	0.212 (1.832)	0.666 (1.225)
Week 18 (n = 31, 4)	0.455 (1.816)	1.043 (1.144)

	GH Treatment-Naive	GH Treatment-Experienced
Week 26 (n = 48, 8)	0.167 (2.016)	0.544 (1.894)

5. Secondary Outcome Measure:

Measure Title	Insulin-like Growth Factor Binding Protein-3 (IGFBP-3) Levels
Measure Description	
Time Frame	Baseline, Week 2, Week 4, Week 8, Week 13, Week 18, Week 26
Safety Issue?	Yes

Analysis Population Description

Safety population consisted of all the participants who received at least 1 dose of study medication and had at least one post-baseline safety assessment. Here "n" signifies number of participants analyzed at that particular time point for each arm group respectively.

Reporting Groups

	Description
GH Treatment-Naive	Growth hormone (GH) Treatment-Naive participants were those who did not receive any prior treatment with Saizen® before initiation of the trial. Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.
GH Treatment-Experienced	Growth hormone (GH) Treatment-experienced participants were those who had undergone treatment with the freeze-dried formulation of Saizen® before initiation of the trial. Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Measured Values

	GH Treatment-Naive	GH Treatment-Experienced
Number of Participants Analyzed	51	8
Insulin-like Growth Factor Binding Protein-3 (IGFBP-3) Levels [units: nmol/L] Mean (Standard Deviation)		
Baseline (n = 51, 8)	124.941 (31.899)	133.375 (36.024)
Week 2 (n = 49, 8)	137.408 (35.088)	162.125 (35.203)

	GH Treatment-Naive	GH Treatment-Experienced
Week 4 (n = 49, 8)	144.592 (32.632)	147.750 (26.451)
Week 8 (n = 50, 8)	147.460 (36.381)	156.625 (36.190)
Week 13 (n = 47, 8)	149.404 (28.272)	151.875 (35.679)
Week 18 (n = 32, 4)	148.813 (39.754)	155.500 (36.235)
Week 26 (n = 49, 8)	152.429 (35.649)	147.500 (30.402)

6. Secondary Outcome Measure:

Measure Title	Number of Participants With Treatment Emergent Adverse Events (TEAEs)
Measure Description	Adverse events (AEs): Any untoward medical occurrence in the form of signs, clinically significant abnormalities in laboratory findings, diseases, symptoms, or worsening of complications. TEAEs: AEs occurring after the first administration of Saizen® solution for injection (on Day 1) up to the scheduled routine post treatment follow-up visit (4 weeks [28 days] after the final administration of Saizen® solution for injection).
Time Frame	Day 1 up to 28 days after last dose of study treatment
Safety Issue?	Yes

Analysis Population Description

Safety population consisted of all the participants who received at least 1 dose of study medication and had at least one post-baseline safety assessment.

Reporting Groups

	Description
Saizen®	Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Measured Values

	Saizen®
Number of Participants Analyzed	59
Number of Participants With Treatment Emergent Adverse Events (TEAEs) [units: participants]	40

Reported Adverse Events

Time Frame	Day 1 up to 28 days after last dose of study treatment
Additional Description	TEAEs: AEs occurring after the first administration of Saizen® solution for injection (on Day 1) up to the scheduled routine post treatment follow-up visit (4 weeks [28 days] after the final administration of Saizen® solution for injection).

Reporting Groups

	Description
Saizen®	Single dose of Saizen® (recombinant human growth hormone, r-hGH) solution for injection will be administered subcutaneously for 26 weeks. Dosage regimen will be in accordance with marketed formulation of Saizen® (freeze-dried formulation), based on locally approved product labeling.

Serious Adverse Events

	Saizen®
	Affected/At Risk (%)
Total	3/59 (5.08%)
Investigations	
Hepatic enzyme increased [A] *	1/59 (1.69%)
Metabolism and nutrition disorders	
Hyponatraemia [A] *	1/59 (1.69%)
Psychiatric disorders	
Anxiety [A] *	1/59 (1.69%)
Depression [A] *	1/59 (1.69%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (14.0)

Other Adverse Events

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

	Saizen®
	Affected/At Risk (%)
Total	13/59 (22.03%)
General disorders	
Oedema peripheral [A] *	5/59 (8.47%)
Infections and infestations	
Nasopharyngitis [A] *	4/59 (6.78%)
Investigations	
Insulin-like growth factor increased [A] *	3/59 (5.08%)
Nervous system disorders	
Headache [A] *	3/59 (5.08%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] *	3/59 (5.08%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (14.0)

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.

Results Point of Contact:

Name/Official Title: Merck KGaA Communication Center
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