ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 03/05/2010

ClinicalTrials.gov ID: NCT00666458

Study Identification

Unique Protocol ID:	D1680C00002
Brief Title:	18-week add-on to Metformin Comparison of Saxagliptin and Sitagliptin in Adult Patients With Type 2 Diabetes (T2D)
Official Title:	18-wk, International, Multi-centre, Randomized, Parallel-group, Double-Blind, Active-Controlled Phase IIIb Study to Evaluate the Efficacy and Safety of Saxagliptin in Combination With Metformin in Comparison With Sitagliptin in Combination With Metformin in Adult Patients With T2D Who Have Inadequate Glycaemic Control on Metformin Alone
Secondary IDs:	EudraCT number 2007-006095-11

Study Status

Record Verification:	March 2010
Overall Status:	Completed
Study Start:	April 2008
Primary Completion:	March 2009 [Actual]
Study Completion:	March 2009 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	
Collaborators:	Bristol-Myers Squibb

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: M34-08 Board Name: Regionala Etikprövningsnämnden i Linköping Board Affiliation: Linköping, Sweden Phone: +46 (0)13 22 17 45 Email: anna.alexandersson@linkoping.epn.se
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	Sweden: The National Board of Health and Welfare Norway: Norwegian Institute of Public Health Denmark: National Board of Health Italy: National Institute of Health France: Direction Générale de la Santé South Africa: Department of Health Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Brazil: Ministry of Health Mexico: Ministry of Health Belgium: Federal Agency for Medicines and Health Products, FAMHP

Study Description

Brief Summary:	Saxagliptin is a new investigational medication being developed for treatment of type 2 diabetes. This study is designed to assess the efficacy and tolerability of saxagliptin in addition to metformin and compare to sitagliptin in addition with metformin.
Detailed Description:	

Conditions

Conditions:	Type 2 Diabetes
Keywords:	Type 2 diabetes metformin

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3

Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	822 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 saxagliptin add-on to metformin	Drug: saxagliptin tablet, per oral, once daily Other Names: • Onglyza
Active Comparator: 2 sitagliptin add-on to metformin	Drug: sitagliptin capsule, per oral, once daily Other Names: • Januvia

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria: • Diagnosed with type 2 diabetes • Treatment with metformin alone on stable doses of 1500 mg or higher per day for at least 8 weeks Exclusion Criteria: • Type 1 diabetes, history of diabetic ketoacidosis or hyperosmolar non-ketotic coma

- Insulin therapy within one year
- Previous treatment with DPP-4 inhibitor

Contacts/Locations

Study Officials: André Scheen, Professor
Study Principal Investigator
Clinical Pharmacology Unit, Liege, Belgium

Peter Öhman, MD, PhD
Study Director
AstraZeneca, Wilmington, USA

Deborah Price, MSc
Study Chair
AstraZeneca, Wilmington, USA

Locations: Argentina
Research Site
Ciudad de Buenos Aires, Argentina

Research Site
Lanus, Buenos Aires, Argentina

Research Site
Mar Del Plata, Buenos Aires, Argentina

Research Site
Buenos Aires, Buenos Aires, Argentina

Research Site
Cordoba, Argentina

Research Site
Rosario, Argentina

Research Site
Santa Fe, Santa Fe, Argentina

Research Site
Caba, Argentina

Research Site
Capital Federal, Argentina

Research Site
Cordoba, Argentina

Belgium
Research Site
Aalst, Belgium, Belgium

Research Site
Bonheiden, Belgium, Belgium

Research Site
Genk, Belgium, Belgium

Research Site
Gozee, Belgium, Belgium

Research Site
Hasselt, Belgium, Belgium

Research Site
Liege, Belgium, Belgium

Research Site
Saint-medard, Belgium, Belgium

Research Site
Sint-gillis-waas, Belgium, Belgium

Research Site
Tessenderlo, Belgium, Belgium

Research Site
Thuillies, Belgium, Belgium

Research Site
Brugge, Belgium

Denmark
Research Site
Aalborg, Denmark

Research Site
Arhus, Denmark

Research Site
Christiansfeld, Denmark

Research Site
Farso, Denmark

Research Site
Gentofte, Denmark

Research Site
Hobro, Denmark

Research Site
Kolding, Denmark

Research Site
Rodovre, Denmark

Research Site
Viborg, Denmark

France
Research Site
Angers, France

Research Site
Chateau Gontier, France

Research Site
Corbeil Essonnes, France

Research Site
La Seyne Sur Mer, France

Research Site
Laval, France

Research Site
Le Lavandou, France

Research Site
Montrevault, France

Research Site
Saint Cyr, France

Research Site
Tierce, France

Research Site
Toulon, France

Research Site
Witry Les Reims, France

Italy
Research Site
Bergamo, BG, Italy

Research Site
Foggia, FG, Italy

Research Site
Chiavari, GE, Italy

Research Site
Genova, GE, Italy

Research Site
Rozzano, MI, Italy

Research Site
Olbia, OT, Italy

Research Site
Padova, PD, Italy

Research Site
Pordenone, PN, Italy

Research Site
Mercato San Severino, SA, Italy

Research Site
Siena, SI, Italy

Mexico
Research Site
Mexico, D.f., Mexico

Research Site
Guadalajara, Jalisco, Mexico

Research Site
Monterrey, Mexico

Norway
Research Site
Alesund, Norway

Research Site
Elverum, Norway

Research Site
Halden, Norway

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Hamar, Norway

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Lierskogen, Norway

Research Site
Lillehammer, Norway

Research Site
Oslo, Norway

Research Site
Sandvika, Norway

Research Site
Strommen, Norway

Research Site
Svelvik, Norway

South Africa
Research Site
Bloemfontein, South Africa

Research Site
Benoni, Gauteng, South Africa

Research Site
Johannesburg, Gauteng, South Africa

Research Site
Kwa Zulu Natal, South Africa

Research Site
Cape Town, South Africa, South Africa

Research Site
Durban, South Africa, South Africa

Research Site
Cape Town, Western Cape, South Africa

Research Site
Durban, South Africa

Research Site
Johannesburg, South Africa

Research Site
Pretoria, South Africa

Sweden
Research Site
Boras, Sweden

Research Site
Degeberga, Sweden

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Finspang, Sweden

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Goteborg, Sweden

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Jonkoping, Sweden

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Odeshog, Sweden

Research Site
Orebro, Sweden

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Pitea, Sweden

Research Site
Rattvik, Sweden

Research Site
Skanor, Sweden

Research Site
Timra, Sweden

Research Site
Trollhattan, Sweden

Research Site
Uddevalla, Sweden

Research Site
Umea, Sweden

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Saxa + Met	Saxagliptin 5 mg tablets added on to open-label metformin
Sita + Met	Sitagliptin 100 mg capsules added on to open-label metformin

Overall Study

	Saxa + Met	Sita + Met
Started	403 [1]	398 [1]
Completed	365 [2]	374 [2]
Not Completed	38	24
Adverse Event	8	7
Withdrawal by Subject	5	4

	Saxa + Met	Sita + Met
Lost to Follow-up	0	3
Administrative reason by sponsor	1	1
Incorrect enrollment	7	1
Study specific discontinuation criteria	14	7
Severe non-compliance to the protocol	1	1
Safety reasons	1	0
Medical history of anemia	1	0

[1] Randomized and treated
[2] Completed 18 weeks of treatment

Baseline Characteristics

Reporting Groups

	Description
Saxa + Met	Saxagliptin 5 mg tablets added on to open-label metformin
Sita + Met	Sitagliptin 100 mg capsules added on to open-label metformin

Baseline Measures

	Saxa + Met	Sita + Met	Total
Number of Participants	403	398	801
Age, Continuous [units: years] Mean (Standard Deviation)	58.77 (10.14)	58.07 (10.51)	58.42 (10.32)
Gender, Male/Female [units: Participants]			
Female	213	196	409
Male	190	202	392

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Hemoglobin A1c (HbA1c) Change From Baseline to Week 18
Measure Description	Adjusted mean change from baseline in HbA1c achieved with saxagliptin added on to metformin versus sitagliptin added on to metformin at Week 18 (Per Protocol Analysis Set). HbA1c is a continuous measure, the change from baseline for each participant is calculated as the Week 18 value minus the baseline value.
Time Frame	Baseline, Week 18
Safety Issue?	No

Analysis Population Description

Randomized participants who completed the 18 weeks of treatment had both baseline and week 18 HbA1c measurement and had no significant protocol deviations.

Reporting Groups

	Description
Saxa + Met	Saxagliptin 5 mg tablets added on to open-label metformin
Sita + Met	Sitagliptin 100 mg capsules added on to open-label metformin

Measured Values

	Saxa + Met	Sita + Met
Number of Participants Analyzed	334	343
Hemoglobin A1c (HbA1c) Change From Baseline to Week 18 [units: Percent] Mean (Standard Error)		
Baseline	7.68 (0.052)	7.69 (0.047)
Week 18	7.16 (0.052)	7.07 (0.051)
Adjusted Change from Baseline	-0.52 (0.039)	-0.62 (0.038)

Statistical Analysis 1 for Hemoglobin A1c (HbA1c) Change From Baseline to Week 18

Statistical Analysis Overview	Comparison Groups	Saxa + Met, Sita + Met
	Comments	[Not specified]

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

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	0.09
	Confidence Interval	(2-Sided) 95% -0.01 to 0.20
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.055
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving Therapeutic Glycaemic Response Defined as HbA1c <= 6.5% at Week 18
Measure Description	Proportion of Patients Achieving Therapeutic Glycaemic Response Defined as HbA1c <= 6.5% at Week 18 (Full Analysis Set)
Time Frame	Week 18 (Last Observation Carried Forward)
Safety Issue?	No

Analysis Population Description

Randomized participants who took at least 1 dose of double-blind treatment. To be included in the Week 18 LOCF analysis, participants must have had a baseline and at least 1 post-baseline measurement.

Reporting Groups

	Description
Saxa + Met	Saxagliptin 5 mg tablets added on to open-label metformin
Sita + Met	Sitagliptin 100 mg capsules added on to open-label metformin

Measured Values

	Saxa + Met	Sita + Met
Number of Participants Analyzed	399	392
Proportion of Patients Achieving Therapeutic Glycaemic Response Defined as HbA1c <= 6.5% at Week 18 [units: Percentage of Participants]	26.3	29.1

Statistical Analysis 1 for Proportion of Patients Achieving Therapeutic Glycaemic Response Defined as HbA1c <= 6.5% at Week 18

Statistical Analysis Overview	Comparison Groups	Saxa + Met, Sita + Met
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Difference in Percent]
	Estimated Value	-2.8
	Confidence Interval	(2-Sided) 95% -9.0 to 3.5
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Fasting Plasma Glucose Change From Baseline to Week 18 (mg/dL)
Measure Description	Adjusted mean change from baseline in Fasting Plasma Glucose achieved with saxagliptin added on to metformin versus sitagliptin added on to metformin at Week 18 (Full Analysis Set). Fasting Plasma Glucose is a continuous measure, the change from baseline for each participant is calculated as the Week 18 (LOCF) value minus the baseline value.
Time Frame	Baseline, Week 18 (Last Observation Carried Forward)
Safety Issue?	No

Analysis Population Description

Randomized participants who took at least 1 dose of double-blind treatment. To be included in analysis of change from baseline to Week 18 LOCF, participants must have had a baseline and at least 1 post-baseline measurement.

Reporting Groups

	Description
Saxa + Met	Saxagliptin 5 mg tablets added on to open-label metformin
Sita + Met	Sitagliptin 100 mg capsules added on to open-label metformin

Measured Values

	Saxa + Met	Sita + Met
Number of Participants Analyzed	397	392
Fasting Plasma Glucose Change From Baseline to Week 18 (mg/dL) [units: mg/dL] Mean (Standard Error)		
Baseline	159.67 (2.280)	160.22 (2.192)
Week 18	149.04 (1.991)	143.94 (1.864)
Adjusted Change from Baseline	-10.75 (1.455)	-16.16 (1.464)

Statistical Analysis 1 for Fasting Plasma Glucose Change From Baseline to Week 18 (mg/dL)

Statistical Analysis Overview	Comparison Groups	Saxa + Met, Sita + Met
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	5.42
	Confidence Interval	(2-Sided) 95% 1.37 to 9.47
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.064
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Fasting Plasma Glucose Change From Baseline to Week 18 (mmol/L)
Measure Description	Adjusted mean change from baseline in Fasting Plasma Glucose achieved with saxagliptin added on to metformin versus sitagliptin added on to metformin at Week 18 (Full Analysis Set). Fasting Plasma Glucose is a continuous measure, the change from baseline for each participant is calculated as the Week 18 (LOCF) value minus the baseline value.
Time Frame	Baseline, Week 18 (Last Observation Carried Forward)

Safety Issue?	No

Analysis Population Description

Randomized participants who took at least 1 dose of double-blind treatment. To be included in analysis of change from baseline to Week 18 LOCF, participants must have had a baseline and at least 1 post-baseline measurement.

Reporting Groups

	Description
Saxa + Met	Saxagliptin 5 mg tablets added on to open-label metformin
Sita + Met	Sitagliptin 100 mg capsules added on to open-label metformin

Measured Values

	Saxa + Met	Sita + Met
Number of Participants Analyzed	397	392
Fasting Plasma Glucose Change From Baseline to Week 18 (mmol/L) [units: mmol/L] Mean (Standard Error)		
Baseline	8.86 (0.127)	8.89 (0.122)
Week 18	8.27 (0.111)	7.99 (0.103)
Adjusted Change from Baseline	-0.60 (0.081)	-0.90 (0.081)

Statistical Analysis 1 for Fasting Plasma Glucose Change From Baseline to Week 18 (mmol/L)

Statistical Analysis Overview	Comparison Groups	Saxa + Met, Sita + Met
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	0.30
	Confidence Interval	(2-Sided) 95% 0.08 to 0.53
	Parameter Dispersion	Type: Standard Error of the mean

		Value: 0.115
	Estimation Comments	[Not specified]

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Saxa + Met	Saxagliptin 5 mg tablets added on to open-label metformin
Sita + Met	Sitagliptin 100 mg capsules added on to open-label metformin

Serious Adverse Events

	Saxa + Met	Sita + Met
	Affected/At Risk (%)	Affected/At Risk (%)
Total	7/403 (1.74%)	5/398 (1.26%)
Cardiac disorders		
Supraventricular Tachycardia [A] †	1/403 (0.25%)	1/398 (0.25%)
Gastrointestinal disorders		
Faecaloma [A] †	1/403 (0.25%)	0/398 (0%)
General disorders		
Chills [A] †	1/403 (0.25%)	0/398 (0%)
Ulcer Haemorrhage [A] †	1/403 (0.25%)	0/398 (0%)
Injury, poisoning and procedural complications		
Fall [A] †	0/403 (0%)	1/398 (0.25%)
ROAD TRAFFIC ACCIDENT [A] †	1/403 (0.25%)	0/398 (0%)
Metabolism and nutrition disorders		

	Saxa + Met	Sita + Met
	Affected/At Risk (%)	Affected/At Risk (%)
Hyperglycaemia [A] †	1/403 (0.25%)	0/398 (0%)
Hypoglycaemia [A] †	0/403 (0%)	1/398 (0.25%)
Hypoglycaemic Unconsciousness [A] †	0/403 (0%)	1/398 (0.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Endometrial Cancer [A] †	1/403 (0.25%)	0/398 (0%)
Respiratory, thoracic and mediastinal disorders		
Asthma [A] †	1/403 (0.25%)	0/398 (0%)
Vascular disorders		
Aortic Aneurysm [A] †	0/403 (0%)	1/398 (0.25%)

† 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%

	Saxa + Met	Sita + Met
	Affected/At Risk (%)	Affected/At Risk (%)
Total	54/403 (13.4%)	50/398 (12.56%)
Infections and infestations		
Influenza [A] †	27/403 (6.7%)	27/398 (6.78%)
Urinary Tract Infection [A] †	28/403 (6.95%)	26/398 (6.53%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

There is NOT 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:

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