ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 01/16/2012

ClinicalTrials.gov ID: NCT01006590

Study Identification

Unique Protocol ID:	D1680L00003
Brief Title:	Efficacy and Tolerability of Saxagliptin add-on Compared to Uptitration of Metformin in Patients With Type 2 Diabetes (PROMPT)
Official Title:	A 24-Week, Randomised, Double-Blind, Active-Controlled, Multi-Centre Phase IIIb/IV Study to Evaluate the Efficacy and Tolerability of Saxagliptin Add-On Compared to Uptitration of Metformin in Patients With Type 2 Diabetes Mellitus With Inadequate Glycaemic Control on Sub-Maximal Doses of Metformin
Secondary IDs:	

Study Status

Record Verification:	January 2012
Overall Status:	Completed
Study Start:	October 2009
Primary Completion:	
Study Completion:	December 2010 [Actual]

Sponsor/Collaborators

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

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: OM003 Board Name: Commission d'Ethique Biomédicale Hospitalo-Facultaire de l'UCL Board Affiliation: Commission d'Ethique Biomédicale Hospitalo-Facultaire de l'UCL Phone: +32 2 764 55 14 Email: commission.ethique@md.ucl.ac.be
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Belgium: Federal Agency for Medicinal Products and Health Products Belgium: Institutional Review Board France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) France: CPP Comité de Protection des Personnes = Ethics Committee Germany: Ethics Commission Germany: Federal Institute for Drugs and Medical Devices (Bfarm) Italy: Ethics Committee Italy: National Monitoring Centre for Clinical Trials - Ministry of Health United Kingdom: Medicines and Healthcare Products Regulatory Agency United Kingdom: National Health Service United Kingdom: Research Ethics Committee Turkey: Regional Ethics Committee Turkey: Ministry of Health Spain: Comité Ético de Investigación Clínica Spain: Spanish Agency of Medicines

Study Description

Brief Summary:	The study will evaluate the efficacy and tolerability of saxagliptin compared to uptitration of metformin in patients with type 2 diabetes who have inadequate glycaemic control on a submaximal dose of metformin.
Detailed Description:	

Conditions

Conditions:	Type 2 Diabetes Mellitus
Keywords:	Type 2 Diabetes Mellitus Saxagliptin Randomised Double-blind

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	286 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1 Saxagliptin 5 mg	Drug: Saxagliptin 5 mg, oral tablet, once daily Other Names: • Onglyza
Active Comparator: 2 Metformin 500 -1000 mg	Drug: Metformin 500 mg, oral tablet, 1 or 2 additional tablets per day added to background therapy Other Names: • Metformin

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Provision of signed informed consent
- Established clinical diagnosis of type 2 diabetes. Treatment with a stable dose of metformin monotherapy (1500-1700 mg/day) for at least 8 weeks prior to visit 1.
- HbA1c ≥7.0% and ≤10.0%

Exclusion Criteria:

- Type 1 diabetes, history of diabetic ketoacidosis or hyperosmolar non-ketonic coma.
- Renal impairment as defined by a creatinine clearance <60 mL/min/1.73 m2
- Individuals who, in the opinion of the investigator, in which participation in this study may pose a significant risk to the patient and could render the patient unable to successfully complete the study

Contacts/Locations

Study Officials:

Locations: Belgium

Research Site
Brussels (woluwe-st-lambert), Belgium, Belgium

Research Site
Halen, Belgium, Belgium

Research Site
Lommel, Belgium, Belgium

Research Site
Oostham, Belgium, Belgium

Research Site
Sint-gillis-waas, Belgium, Belgium

Research Site
Zoersel, Belgium, Belgium

Research Site
Brugge, Belgium

Research Site
Moerkerke, Belgium

Research Site
Tielt, Belgium

France
Research Site
Chatellerault, France

Research Site
Corbeil Essonnes, France

Research Site
La Rochelle, France

Research Site
La Seyne Sur Mer, France

Research Site
Paris, France

Research Site
Seysses, France

Research Site
Tierce, France

Germany
Research Site
Berlin, Germany

Research Site
Freiburg, Germany

Research Site
Leipzig, Germany

Research Site
Ludwigshafen, Germany

Research Site
Mannheim, Germany

Research Site
Rhaunen, Germany

Research Site
Schmiedeberg, Germany

Research Site
Wahlstedt, Germany

United Kingdom
Research Site
Reading, Berks, United Kingdom

Research Site
Atherstone, Warwickshire, United Kingdom

Research Site
Leamington Spa, Warwks, United Kingdom

Research Site
Warminster, Wiltshire, United Kingdom

Research Site
Westbury, Wiltshire, United Kingdom

Research Site
Ashford, United Kingdom

Research Site
Bath, United Kingdom

Research Site
Coventry, United Kingdom

Research Site
Peterborough, United Kingdom

Italy
Research Site
Bergamo, BG, Italy

Research Site
Forli, FC, Italy

Research Site
Milano, MI, Italy

Research Site
Padova, PD, Italy

Research Site
Pordenone, PN, Italy

Research Site
Siena, SI, Italy

Research Site
Roma, Italy

Spain
Research Site
Sevilla, Andalucia, Spain

Research Site
Oviedo, Asturias, Spain

Research Site
Barcelona, Cataluna, Spain

Research Site
Madrid, Comunidad de Madrid, Spain

Research Site
San Sebastian de Los Reyes, Comunidad de Madrid, Spain

Research Site
Alicante, Comunidad Valenciana, Spain

Research Site
A Coruna, Galicia, Spain

Turkey
Research Site
Ankara, Turkey, Turkey

Research Site
Bursa, Turkey, Turkey

Research Site
Kirikkale, Turkey, Turkey

Research Site
Ankara, Turkey

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	The study was conducted at hospital clinics and general practitioners. Patient recruitment started October 20, 2009 and was completed April 30, 2010
Pre-Assignment Details	Screening, enrollment (2 weeks) and lead-in period (4 weeks). Main reason for not being randomised was due to renal function not meeting inclusion criteria. (Samples taken and analysed after enrollment into the study but prior to randomisation).

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Overall Study

	Saxagliptin	Metformin Uptitration
Started	147 [1]	139 [1]
Completed	119 [2]	107 [2]
Not Completed	28	32
Adverse Event	2	3
Death	1	1
Lost to Follow-up	1	1

	Saxagliptin	Metformin Uptitration
Protocol Violation	1	0
Withdrawal by Subject	4	2
Study specific discontinuation criteria	16	23
Not specified	3	2

[1] Randomised and treated
[2] Completed 24 weeks of treatment

Baseline Characteristics

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Baseline Measures

	Saxagliptin	Metformin Uptitration	Total
Number of Participants	147	139	286
Age, Continuous [units: Years] Mean (Standard Deviation)	58.7 (11.31)	58.6 (9.79)	58.7 (10.58)
Gender, Male/Female [units: Participants]			
Female	59	63	122
Male	88	76	164

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Absolute Change From Baseline in HbA1c at Week 24
Measure Description	
Time Frame	Baseline and 24 weeks

Safety Issue?	No
Anticipated Reporting Date	November 2011

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Measured Values

	Saxagliptin	Metformin Uptitration
Number of Participants Analyzed	146	137
Absolute Change From Baseline in HbA1c at Week 24 [units: Percent (%)] Mean (Standard Error)	-0.47 (0.06)	-0.38 (0.06)

Statistical Analysis 1 for Absolute Change From Baseline in HbA1c at Week 24

Statistical Analysis Overview	Comparison Groups	Saxagliptin, Metformin Uptitration
	Comments	The null hypothesis H0: μt-μC=0, where μT denotes the mean absolute change in HbA1c from baseline to Week 24 in the group of patients treated with saxagliptin (test medication, T) and μC the mean absolute change in HbA1c from baseline to Week 24 in the group of patients with uptitration of metformin (comparator, C) A sample size of 120 randomized and treated patients per treatment group yielded 80% power under the assumption of a true treatment difference of 0.4% and a standard deviation of 1.1%
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.26
	Comments	[Not specified]
	Method	ANCOVA
	Comments	With baseline value as covariate and treatment group as factor; comparison of LSmeans for treatment

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.10
	Confidence Interval	(2-Sided) 95% -0.26 to 0.07
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.09
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving a Therapeutic Response at Week 24 Defined as HbA1c<7.0%
Measure Description	Proportion, percentage of patients in each treatment group, achieving therapeutic response, HbA1c below 7.0 percent
Time Frame	24 Weeks
Safety Issue?	No
Anticipated Reporting Date	November 2011

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Measured Values

	Saxagliptin	Metformin Uptitration
Number of Participants Analyzed	146	137
Proportion of Patients Achieving a Therapeutic Response at Week 24 Defined as HbA1c<7.0% [units: Percentage of patients]	43.8	35.0

Statistical Analysis 1 for Proportion of Patients Achieving a Therapeutic Response at Week 24 Defined as HbA1c<7.0%

Statistical Analysis Overview	Comparison Groups	Saxagliptin, Metformin Uptitration
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3202
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	5.8
	Confidence Interval	(2-Sided) 95% -5.6 to 17.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.79
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving a Therapeutic Response at Week 24 Defined as HbA1c<=6.5%
Measure Description	Proportion, percentage of patients in each treatment group, achieving therapeutic response, HbA1c below or equal to 6.5 percent
Time Frame	24 Weeks
Safety Issue?	No
Anticipated Reporting Date	November 2011

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day

	Description
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Measured Values

	Saxagliptin	Metformin Uptitration
Number of Participants Analyzed	146	137
Proportion of Patients Achieving a Therapeutic Response at Week 24 Defined as HbA1c<=6.5% [units: Percentage of patients]	20.5	16.8

Statistical Analysis 1 for Proportion of Patients Achieving a Therapeutic Response at Week 24 Defined as HbA1c<=6.5%

Statistical Analysis Overview	Comparison Groups	Saxagliptin, Metformin Uptitration
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6203
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	2.3
	Confidence Interval	(2-Sided) 95% -6.7 to 11.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.58
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Fasting Plasma Glucose

Measure Description	
Time Frame	Baseline and 24 weeks
Safety Issue?	No
Anticipated Reporting Date	November 2011

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Measured Values

	Saxagliptin	Metformin Uptitration
Number of Participants Analyzed	146	137
Change From Baseline to Week 24 in Fasting Plasma Glucose [units: millimol/Liter] Mean (Standard Error)	-1.07 (0.16)	-1.14 (0.17)

Statistical Analysis 1 for Change From Baseline to Week 24 in Fasting Plasma Glucose

Statistical Analysis Overview	Comparison Groups	Saxagliptin, Metformin Uptitration
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7627
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	0.07
	Confidence Interval	(2-Sided) 95% -0.38 to 0.52
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.23
	Estimation Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Fasting Insulin
Measure Description	
Time Frame	Baseline and 24 weeks
Safety Issue?	No
Anticipated Reporting Date	November 2011

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Measured Values

	Saxagliptin	Metformin Uptitration
Number of Participants Analyzed	146	137
Change From Baseline to Week 24 in Fasting Insulin [units: microUnit/milliLiter] Mean (Standard Error)	-1.9 (0.82)	-2.3 (0.85)

Statistical Analysis 1 for Change From Baseline to Week 24 in Fasting Insulin

Statistical Analysis Overview	Comparison Groups	Saxagliptin, Metformin Uptitration
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7701
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	0.3
	Confidence Interval	(2-Sided) 95% -2.0 to 2.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.19
	Estimation Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in Beta-cell Function as Measured by Homeostasis Model Assessment-2-beta
Measure Description	
Time Frame	Baseline and 24 weeks
Safety Issue?	No
Anticipated Reporting Date	November 2011

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day

	Description
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Measured Values

	Saxagliptin	Metformin Uptitration
Number of Participants Analyzed	146	137
Change From Baseline to Week 24 in Beta-cell Function as Measured by Homeostasis Model Assessment-2-beta [units: Percent (%)] Mean (Standard Error)	4.70 (3.01)	2.34 (3.13)

Statistical Analysis 1 for Change From Baseline to Week 24 in Beta-cell Function as Measured by Homeostasis Model Assessment-2-beta

Statistical Analysis Overview	Comparison Groups	Saxagliptin, Metformin Uptitration
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5882
	Comments	[Not specified]
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	2.39
	Confidence Interval	(2-Sided) 95% -6.22 to 10.93
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.34
	Estimation Comments	[Not specified]

Reported Adverse Events

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

Reporting Groups

	Description
Saxagliptin	Saxagliptin, 5 mg once daily add-on to Metformin 1500 mg/day
Metformin Uptitration	Metformin uptitration, 500-1000 mg daily , add-on to Metformin 1500 mg/day

Serious Adverse Events

	Saxagliptin	Metformin Uptitration
	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/147 (4.08%)	6/139 (4.32%)
Cardiac disorders		
Atrioventricilar Block Second Degree [A] †	0/147 (0%)	1/139 (0.72%)
Palpitations [A] †	1/147 (0.68%)	0/139 (0%)
Hepatobiliary disorders		
Cholecystitis [A] †	1/147 (0.68%)	0/139 (0%)
Infections and infestations		
Gastroenteritis [A] †	0/147 (0%)	1/139 (0.72%)
Pneumonia [A] †	0/147 (0%)	1/139 (0.72%)
Metabolism and nutrition disorders		
Obesity [A] †	0/147 (0%)	1/139 (0.72%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	1/147 (0.68%)	0/139 (0%)
Osteoarthritis [A] †	0/147 (0%)	1/139 (0.72%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		

	Saxagliptin	Metformin Uptitration
	Affected/At Risk (%)	Affected/At Risk (%)
Prostate Cancer [A] †	1/147 (0.68%)	0/139 (0%)
Tongue Neoplasm Malignant Stage Unspecified [A] †	0/147 (0%)	1/139 (0.72%)
Nervous system disorders		
Nerve Root Compression [A] †	1/147 (0.68%)	0/139 (0%)
Vascular disorders		
Aortic Dissection [A] †	1/147 (0.68%)	0/139 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 13.1

Other Adverse Events

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

	Saxagliptin	Metformin Uptitration
	Affected/At Risk (%)	Affected/At Risk (%)
Total	27/147 (18.37%)	22/139 (15.83%)
Gastrointestinal disorders		
Diarrhoea [A] †	9/147 (6.12%)	17/139 (12.23%)
Infections and infestations		
Nasopharyngitis [A] †	8/147 (5.44%)	2/139 (1.44%)
Metabolism and nutrition disorders		
Hypoglycaemia [A] †	10/147 (6.8%)	3/139 (2.16%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 13.1

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

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