ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 09/27/2013

ClinicalTrials.gov ID: NCT01006603

Study Identification

Unique Protocol ID:	D1680L00002
Brief Title:	Saxagliptin Compared to Glimepiride in Elderly Type 2 Diabetes Patients, With Inadequate Glycemic Control on Metformin (GENERATION)
Official Title:	A 52-Week, Randomised, Double Blind, Active-Controlled, Multi-Centre Phase IIIb/IV Study to Evaluate the Efficacy and Tolerability of Saxagliptin Compared to Glimepiride in Elderly Patients With Type 2 Diabetes Mellitus Who Have Inadequate Glycaemic Control on Metformin Monotherapy
Secondary IDs:	

Study Status

Record Verification:	September 2013
Overall Status:	Completed
Study Start:	October 2009
Primary Completion:	June 2012 [Actual]
Study Completion:	June 2012 [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: M146-09 Board Name: Regionala etikprövningsnämnden i Linköping Board Affiliation: Regionala etikprövningsnämnden i Linköping Phone: +46 13 22 70 30 Email: anna.alexandersson@linkoping.epn.se
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Austria: Agency for Health and Food Safety Denmark: Danish Dataprotection Agency Denmark: Danish Medicines Agency Denmark: Ethics Committee Finland: Ethics Committee Finland: Finnish Medicines Agency France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) France: Institutional Ethical Committee Germany: Ethics Commission Germany: Federal Institute for Drugs and Medical Devices Greece: Ethics Committee Greece: Ministry of Health and Welfare Greece: National Organization of Medicines Italy: Ethics Committee Italy: National Monitoring Centre for Clinical Trials - Ministry of Health Norway: Data Protection Authority Norway: Norwegian Medicines Agency Norway:National Committee for Medical and Health Research Ethics Spain: Comité Ético de Investigación Clínica Spain: Spanish Agency of Medicines Sweden: Medical Products Agency Sweden: Regional Ethical Review Board United Kingdom: Medicines and Healthcare Products Regulatory Agency United Kingdom: National Health Service United Kingdom: Research Ethics Committee

Study Description

Brief Summary: This study will evaluate the efficacy and tolerability of saxagliptin compared to glimepiride in elderly patients with type 2 diabetes mellitus who have inadequate glycaemic control on metformin monotherapy.

Detailed Description:

Conditions

Conditions: Type 2 Diabetes Mellitus

Keywords: Type 2 Diabetes Mellitus
elderly patients
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, Investigator)

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 957 [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	Drug: Glimepiride

Arms	Assigned Interventions
Glimepiride 1 - 6 mg	1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily Other Names: • Amaryl

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 65 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Provision of informed consent prior to any study specific procedures
- Established clinical diagnosis of type 2 diabetes. Treatment with a stable metformin monotherapy, for at least 8 weeks prior to Visit 1
- HbA1c ≥7.0% and ≤9.0%

Exclusion Criteria:

- Type 1 diabetes, history of diabetic ketoacidosis or hyperosmolar non-ketonic coma. Current use of any injectable or oral antihyperglycemic agent excluding metformin.
- Renal impairment as defined by a creatinine clearance <60 mL/min
- 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: Austria
Research Site
Feldbach, Austria

Research Site
Graz, Austria

Research Site
Salzburg, Austria

Research Site
Vienna, Austria

Research Site
Wien, Austria

Denmark
Research Site
Aalborg, Denmark

Research Site
Ans by, Denmark

Research Site
Kjellerup, Denmark

Research Site
Kolding, Denmark

Research Site
Norresundby, Denmark

Research Site
Roskilde, Denmark

Research Site
Roslev, Denmark

Research Site
Vaerlose, Denmark

Research Site
Viborg, Denmark

Research Site
Viby J, Denmark

Finland
Research Site
Harjavalta, Finland

Research Site
Helsinki, Finland

Research Site
Kuopio, Finland

Research Site
Kuusankoski, Finland

Research Site
Lahti, Finland, Finland

Research Site
Oulu, Finland

Research Site
Seinajoki, Finland

Research Site
Sipoo, Finland

Research Site
Tampere, Finland

Research Site
Turku, Finland

Research Site
Vantaa, Finland, Finland

Research Site
Vimpeli, Finland

France
Research Site
Chatellerault, France

Research Site
La Rochelle, France

Research Site
La Seyne Sur Mer, France

Research Site
Laval, France

Research Site
Seysses, France

Research Site
Strasbourg, France

Research Site
Tierce, France

Germany
Research Site
Augsburg, Germany

Research Site
Darmstadt, Germany

Research Site
Dresden, Germany

Research Site
Essen, Germany

Research Site
Gelnhausen, Germany

Research Site
Hamburg, HH, Germany

Research Site
Hamburg, Germany

Research Site
Magdeburg, Germany

Research Site
Mayen, Germany

Research Site
Munchen, Germany

Research Site
Neumunster, Germany

Research Site
Nurnberg, Germany

Research Site
Pirna, Germany

Research Site
Ratzeburg, Germany

Research Site
Reinfeld, Germany

Research Site
Sulzbach, Germany

United Kingdom
Research Site
Annan, Dumfries and Galloway, United Kingdom

Research Site
Ayrshire, United Kingdom

Research Site
Barnstaple, Devon, United Kingdom

Research Site
Bath, United Kingdom

Research Site
Bradford-on-avon, Wiltshire, United Kingdom

Research Site
Canterbury, Kent, United Kingdom

Research Site
Cumbernauld, United Kingdom

Research Site
Dundee, United Kingdom

Research Site
Fowey, Cornwall, United Kingdom

Research Site
Frome, Somerset, United Kingdom

Research Site
Hamilton, United Kingdom

Research Site
Middlesex, United Kingdom

Research Site
Motherwell, United Kingdom

Research Site
Nr Penzance, Cornwall, United Kingdom

Research Site
Penzance, Cornwall, United Kingdom

Research Site
Plymouth, Devon, United Kingdom

Research Site
Somerset, United Kingdom

Research Site
Trowbridge, Wiltshire, United Kingdom

Research Site
Wellingborough, United Kingdom

Research Site
Whitstable, Kent, United Kingdom

Greece
Research Site
Athens, Greece, Greece

Research Site
Athens, Greece

Research Site
Nikea, Greece

Research Site
Thessaloniki, Greece

Hungary
Research Site
ACS, Hungary

Research Site
Balatonfured, Hungary

Research Site
Budapest, Hungary

Research Site
ERD, Hungary

Research Site
Gyongyos, Hungary

Research Site
Komarom, Hungary

Italy
Research Site
Chieti, Italy

Research Site
Milano, MI, Italy

Research Site
Napoli, Italy

Research Site
Padova, PD, Italy

Research Site
Palermo, PA, Italy

Research Site
Pordenone, PN, Italy

Research Site
Reggio Emilia, RE, Italy

Research Site
Roma, Italy

Research Site
Viterbo, Italy

Mexico
Research Site
Durango, Durango, Mexico

Research Site
Guadalajara, Jalisco, Mexico

Research Site
Monterrey, Nuevo Leon, Mexico

Norway
Research Site
Aksdal, Norway

Research Site
Alesund, Norway

Research Site
Elverum, Norway

Research Site
Halden, Norway

Research Site
Hamar, Norway

Research Site
Kirkenaer, Norway

Research Site
Larvik, Norway

Research Site
Lierskogen, Norway

Research Site
Nord-lenangen, Norway

Research Site
Oslo, Norway

Research Site
ROA, Norway

Research Site
Sandvika, Norway

Research Site
Skedsmokorset, Norway

Research Site
Sorumsand, Norway

Research Site
Svelvik, Norway

Research Site
Trondheim, Norway

Research Site
Ulset, Norway

Research Site
Kongsvinger, Norway

Spain
Research Site
A Coruna, Galicia, Spain

Research Site
Alicante, Comunidad Valenciana, Spain

Research Site
Begonte (lugo), Galicia, Spain

Research Site
Getafe, Comunidad de Madrid, Spain

Research Site
Madrid, Comunidad de Madrid, Spain

Research Site
Oviedo, Asturias, Spain

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

Research Site
Sevilla, Andalucia, Spain

Research Site
Zamora, Castilla Y Leon, Spain

Sweden
Research Site
Finspang, Sweden

Research Site
Gavle, Sweden

Research Site
Goteborg, Sweden

Research Site
Jarfalla, Sweden

Research Site
Jonkoping, Sweden, Sweden

Research Site
Lessebo, Sweden

Research Site
Lund, Sweden

Research Site
Odeshog, Sweden

Research Site
Pitea, Sweden

Research Site
Rattvik, Sweden

Research Site
Stockholm, Sweden

Research Site
Trollhattan, Sweden

Research Site
Vastervik, Sweden

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Recruitment Details	In total, 152 study centres in 13 countries recruited patients in this study. The first patient was enrolled in the study on 20 October 2009, and the last patient completed the study on 14 June 2012. 957 subjects were enrolled. 753 were deemed eligible for lead-in and 720 were randomized.
Pre-Assignment Details	A 2-week single-blind (to patient only) placebo lead-in period occurred from Week -2 to Week 0. Patients were from this period on,counselled on dietary and lifestyle modifications according to usual clinical routine. They were given a glucometer to check their plasma glucose at home at least every second day.

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride : 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Overall Study

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Started	360 [1]	360 [1]
Completed	289	285
Not Completed	71	75
Withdrawal by Subject	17	19
Lost to Follow-up	0	1
Safety reason	1	1
Protocol Violation	1	3
Incorrect enrolment	0	2
Adverse Event	15	7
Death	1	1
Study specific discontinuation criteria	33	34
Other	3	7

[1] Completed lead-in period and were randomised

Baseline Characteristics

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Baseline Measures

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg	Total
Number of Participants	360	360	720
Age, Categorical [units: participants]			
<=18 years	0	0	0
Between 18 and 65 years	0	0	0
>=65 years	360	360	720
Age, Continuous [units: years] Mean (Standard Deviation)	72.5 (5.72)	72.7 (5.44)	72.6 (5.58)
Gender, Male/Female [units: participants]			
Female	143	132	275
Male	217	228	445
Region of Enrollment [units: participants]			
Greece	21	18	39
Finland	24	19	43
Spain	31	25	56
Austria	30	15	45
United Kingdom	39	49	88
Italy	12	12	24
France	11	13	24
Hungary	9	9	18

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg	Total
Mexico	10	7	17
Denmark	16	17	33
Germany	44	55	99
Norway	47	59	106
Sweden	66	62	128

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Proportion of Patients Reaching HbA1c <7% After 52 Weeks of Treatment Without Confirmed or Severe Hypoglycaemia.
Measure Description	Defined as obtained on or before the 8th day after the last dosing day, as determined by central laboratory. Safety analysis set. Confirmed hypoglycaemia defined as: any event defined as either a symptomatic event with blood glucose level <3 mmol/L (<54 mg/dL) and no need for external assistance, or an asymptomatic blood glucose measurement <3 mmol/L (<54 mg/dL). Major (or severe) hypoglycaemia defined as: symptomatic events requiring external assistance due to severe impairment in consciousness or behaviour, with or without blood glucose level <3 mmol/L (<54 mg/dL), but with prompt recovery after glucose or glucagon administration. These events may be associated with sufficient neuroglycopenia to induce seizure or coma. Plasma glucose measurements may not be available during such an event, but neurological recovery, attributable to the restoration of plasma glucose to normal, was considered sufficient evidence that the event was induced by a low plasma glucose concentration.
Time Frame	From week 0 to week 52.
Safety Issue?	Yes

Analysis Population Description

Safety analysis set (a subset of the randomised analysis set including patients who took at least one investigational product dose).

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Measured Values

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Number of Participants Analyzed	359	359
Proportion of Patients Reaching HbA1c <7% After 52 Weeks of Treatment Without Confirmed or Severe Hypoglycaemia. [units: percentage of participants]		
All patients	37.9	38.2
patients aged <75 years (n=217, n=216)	39.2	33.3
patients aged ≥75 years (n=142, n=143)	35.9	45.5

2. Secondary Outcome Measure:

Measure Title	Proportion of Patients Having Experienced at Least One Hypoglycaemic Event (Confirmed or Severe) Over the 52-week Double-blind Treatment Period.
Measure Description	Hypoglyceamic event defined as, Confirmed hypoglycaemia: any event defined as either a symptomatic event with blood glucose level <3 mmol/L (<54 mg/dL) and no need for external assistance, or an asymptomatic blood glucose measurement <3 mmol/L (<54 mg/dL). Major (or severe) hypoglycaemia: symptomatic events requiring external assistance due to severe impairment in consciousness or behaviour, with or without blood glucose level <3 mmol/L (<54 mg/dL), but with prompt recovery after glucose or glucagon administration. These events may be associated with sufficient neuroglycopenia to induce seizure or coma. Plasma glucose measurements may not be available during such an event, but neurological recovery, attributable to the restoration of plasma glucose to normal, was considered sufficient evidence that the event was induced by a low plasma glucose concentration. Safety analysis set.
Time Frame	From week 0 to week 52.
Safety Issue?	Yes

Analysis Population Description

Safety analysis set (a subset of the randomised analysis set including patients who took at least one investigational product dose).

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Measured Values

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Number of Participants Analyzed	359	359
Proportion of Patients Having Experienced at Least One Hypoglycaemic Event (Confirmed or Severe) Over the 52-week Double-blind Treatment Period. [units: percentage of patients]	1.1	15.3

3. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 52 in HbA1c.
Measure Description	Measured as the difference between the last on-treatment value (defined as obtained before or on the 8th day after the last dosing date), and the last pre-randomisation HbA1c value, as determined by central laboratory. Full analysis set.
Time Frame	From week 0 to week 52.
Safety Issue?	No

Analysis Population Description

The number of subjects with non-missing baseline and Week 52 (LOCF) values in the full analysis set (defined as the subset of patients in the randomized analysis set who took at least one randomised IP dose and have non-missing baseline and post-baseline efficacy data for at least one variable).

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Measured Values

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Number of Participants Analyzed	353	345
Change From Baseline to Week 52 in HbA1c. [units: % of glycosylated hemoglobin] Mean (95% Confidence Interval)	-0.44 (-0.51 to -0.37)	-0.64 (-0.71 to -0.57)

4. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving a Therapeutic Glycaemic Response at Week 52 Defined as HbA1c <7.0%
Measure Description	Proportion of patients with their last on-treatment value (defined as obtained before or on the 8th day after the last dosing date), as determined by central laboratory, below the specified limits. Full analysis set.
Time Frame	From week 0 to week 52
Safety Issue?	No

Analysis Population Description

The number of subjects with non-missing baseline and Week 52 (LOCF) values in the full analysis set (defined as the subset of patients in the randomized analysis set who took at least one randomised IP dose and have non-missing baseline and post-baseline efficacy data for at least one variable).

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Measured Values

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Number of Participants Analyzed	356	353
Proportion of Patients Achieving a Therapeutic Glycaemic Response at Week 52 Defined as HbA1c <7.0% [units: percentage of responders]	44.7	54.7

5. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 52 in Fasting Plasma Glucose (FPG)
Measure Description	Measured as the difference between the last on-treatment value (defined as obtained before or on the first day after the last dosing date)and the last pre-randomisation fasting plasma glucose value, as determined by central laboratory. Full analysis set.
Time Frame	From week 0 to week 52
Safety Issue?	No

Analysis Population Description

The number of subjects with non-missing baseline and Week 52 (LOCF) values in the full analysis set (defined as the subset of patients in the randomized analysis set who took at least one randomised IP dose and have non-missing baseline and post-baseline efficacy data for at least one variable).

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Measured Values

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Number of Participants Analyzed	344	339
Change From Baseline to Week 52 in Fasting Plasma Glucose (FPG) [units: mmol/L] Mean (95% Confidence Interval)	-0.73 (-0.89 to -0.57)	-1.29 (-1.45 to -1.13)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 52 in Insulin
Measure Description	Measured as the difference between the last on-treatment value (defined as obtained before or on the first day after the last dosing date) and the last pre-randomisation fasting plasma insulin value, as determined by central laboratory. Full analysis set.
Time Frame	From week 0 to week 52
Safety Issue?	No

Analysis Population Description

The number of subjects with non-missing baseline and Week 52 (LOCF) values in the full analysis set (defined as the subset of patients in the randomized analysis set who took at least one randomised IP dose and have non-missing baseline and post-baseline efficacy data for at least one variable).

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Measured Values

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Number of Participants Analyzed	312	309

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Change From Baseline to Week 52 in Insulin [units: µU/mL] Mean (95% Confidence Interval)	-2.0 (-3.1 to -1.0)	-0.6 (-1.6 to 0.5)

7. Secondary Outcome Measure:

Measure Title	Change From Baseline to Week 52 in β-cell Function (as Measured by Homeostasis Model Assessment-β [HOMA-β]
Measure Description	β-cell function as estimated by the homeostasis model assessment (HOMA) model. Value is derived from FPG and fasting insulin; fasting insulin values below 2.074 µU/mL or above 57.595 µU/mL and FPG values below 3 mmol/L or above 25 mmol/L are excluded (as restricted by the calculation method used). Full analysis set.
Time Frame	From week 0 to week 52
Safety Issue?	No

Analysis Population Description

The number of subjects with non-missing baseline and Week 52 (LOCF) values in the full analysis set (defined as the subset of patients in the randomized analysis set who took at least one randomised IP dose and have non-missing baseline and post-baseline efficacy data for at least one variable).

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Measured Values

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
Number of Participants Analyzed	240	247
Change From Baseline to Week 52 in β-cell Function (as Measured by Homeostasis Model Assessment-β [HOMA-β] [units: percentage of change from baseline] Mean (95% Confidence Interval)	3.83 (0.79 to 6.88)	16.22 (13.23 to 19.20)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	The at Risk population includes only those randomized subjects who took at least one dose of study drug.

Reporting Groups

	Description
Saxagliptin 5 mg	Saxagliptin 5 mg, oral tablet, once daily
Glimepiride 1 - 6 mg	Glimepiride 1, 2, 3, 4 or 6 mg, oral encapsulated tablet, once daily

Serious Adverse Events

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Total	41/359 (11.42%)	32/359 (8.91%)
Blood and lymphatic system disorders		
ANAEMIA [A] †	1/359 (0.28%)	0/359 (0%)
LYMPHADENOPATHY [A] †	0/359 (0%)	1/359 (0.28%)
Cardiac disorders		
ACUTE MYOCARDIAL INFARCTION [A] †	0/359 (0%)	2/359 (0.56%)
ANGINA PECTORIS [A] †	1/359 (0.28%)	1/359 (0.28%)
ANGINA UNSTABLE [A] †	1/359 (0.28%)	0/359 (0%)
ATRIAL FIBRILLATION [A] †	2/359 (0.56%)	1/359 (0.28%)
CARDIAC FAILURE [A] †	1/359 (0.28%)	3/359 (0.84%)
ISCHAEMIC CARDIOMYOPATHY [A] †	1/359 (0.28%)	0/359 (0%)
MYOCARDIAL INFARCTION [A] †	3/359 (0.84%)	1/359 (0.28%)
PERICARDITIS [A] †	1/359 (0.28%)	0/359 (0%)
TACHYCARDIA [A] †	0/359 (0%)	1/359 (0.28%)
Gastrointestinal disorders		

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
	Affected/At Risk (%)	Affected/At Risk (%)
EPIGASTRIC DISCOMFORT [A] †	1/359 (0.28%)	0/359 (0%)
HIATUS HERNIA [A] †	1/359 (0.28%)	0/359 (0%)
INGUINAL HERNIA [A] †	1/359 (0.28%)	0/359 (0%)
MELAENA [A] †	1/359 (0.28%)	0/359 (0%)
SUBILEUS [A] †	0/359 (0%)	1/359 (0.28%)
General disorders		
CHEST PAIN [A] †	1/359 (0.28%)	0/359 (0%)
DEATH [A] †	0/359 (0%)	1/359 (0.28%)
DEVICE DISLOCATION [A] †	1/359 (0.28%)	0/359 (0%)
INFLAMMATION [A] †	1/359 (0.28%)	0/359 (0%)
Hepatobiliary disorders		
CHOLECYSTITIS [A] †	1/359 (0.28%)	0/359 (0%)
Immune system disorders		
ANAPHYLACTIC SHOCK [A] †	1/359 (0.28%)	0/359 (0%)
Infections and infestations		
APPENDICITIS [A] †	1/359 (0.28%)	0/359 (0%)
DIVERTICULITIS [A] †	0/359 (0%)	1/359 (0.28%)
GASTROENTERITIS [A] †	0/359 (0%)	1/359 (0.28%)
GASTROENTERITIS NOROVIRUS [A] †	0/359 (0%)	1/359 (0.28%)
INFECTIOUS PLEURAL EFFUSION [A] †	0/359 (0%)	1/359 (0.28%)
LABYRINTHITIS [A] †	0/359 (0%)	1/359 (0.28%)
PNEUMONIA [A] †	3/359 (0.84%)	3/359 (0.84%)
PYELONEPHRITIS [A] †	1/359 (0.28%)	0/359 (0%)

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
	Affected/At Risk (%)	Affected/At Risk (%)
RESPIRATORY TRACT INFECTION [A] †	0/359 (0%)	1/359 (0.28%)
URINARY TRACT INFECTION [A] †	0/359 (0%)	1/359 (0.28%)
UROSEPSIS [A] †	1/359 (0.28%)	0/359 (0%)
Injury, poisoning and procedural complications		
ANKLE FRACTURE [A] †	0/359 (0%)	1/359 (0.28%)
CONCUSSION [A] †	1/359 (0.28%)	0/359 (0%)
CONTUSION [A] †	0/359 (0%)	1/359 (0.28%)
FEMUR FRACTURE [A] †	1/359 (0.28%)	0/359 (0%)
HAND FRACTURE [A] †	1/359 (0.28%)	0/359 (0%)
LUMBAR VERTEBRAL FRACTURE [A] †	2/359 (0.56%)	0/359 (0%)
MUSCLE RUPTURE [A] †	0/359 (0%)	1/359 (0.28%)
Investigations		
MEDICAL OBSERVATION [A] †	0/359 (0%)	1/359 (0.28%)
WEIGHT DECREASED [A] †	1/359 (0.28%)	0/359 (0%)
Metabolism and nutrition disorders		
HYPERKALAEMIA [A] †	1/359 (0.28%)	0/359 (0%)
HYPOGLYCAEMIA [A] †	0/359 (0%)	1/359 (0.28%)
Musculoskeletal and connective tissue disorders		
ARTHRALGIA [A] †	1/359 (0.28%)	0/359 (0%)
BACK PAIN [A] †	1/359 (0.28%)	0/359 (0%)
INTERVERTEBRAL DISC PROTRUSION [A] †	0/359 (0%)	1/359 (0.28%)
JOINT EFFUSION [A] †	0/359 (0%)	1/359 (0.28%)

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
	Affected/At Risk (%)	Affected/At Risk (%)
OSTEOARTHRITIS [A] †	1/359 (0.28%)	0/359 (0%)
SPINAL COLUMN STENOSIS [A] †	1/359 (0.28%)	0/359 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
BASAL CELL CARCINOMA [A] †	1/359 (0.28%)	1/359 (0.28%)
BLADDER TRANSITIONAL CELL CARCINOMA [A] †	1/359 (0.28%)	0/359 (0%)
BREAST CANCER [A] †	2/359 (0.56%)	0/359 (0%)
BREAST CANCER IN SITU [A] †	1/359 (0.28%)	0/359 (0%)
COLON CANCER [A] †	1/359 (0.28%)	0/359 (0%)
HEPATIC NEOPLASM MALIGNANT [A] †	1/359 (0.28%)	0/359 (0%)
LUNG CANCER METASTATIC [A] †	0/359 (0%)	1/359 (0.28%)
LYMPHOMA [A] †	1/359 (0.28%)	0/359 (0%)
PANCREATIC CARCINOMA [A] †	1/359 (0.28%)	0/359 (0%)
PROSTATE CANCER [A] †	0/359 (0%)	1/359 (0.28%)
SALIVARY GLAND CANCER [A] †	1/359 (0.28%)	0/359 (0%)
Nervous system disorders		
CEREBROVASCULAR ACCIDENT [A] †	0/359 (0%)	1/359 (0.28%)
EPILEPSY [A] †	0/359 (0%)	1/359 (0.28%)
SYNCOPE [A] †	1/359 (0.28%)	1/359 (0.28%)
TRANSIENT ISCHAEMIC ATTACK [A] †	0/359 (0%)	1/359 (0.28%)
Renal and urinary disorders		
CALCULUS BLADDER [A] †	1/359 (0.28%)	0/359 (0%)
CALCULUS URETERIC [A] †	0/359 (0%)	1/359 (0.28%)

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
	Affected/At Risk (%)	Affected/At Risk (%)
NEUROGENIC BLADDER [A] †	0/359 (0%)	1/359 (0.28%)
Respiratory, thoracic and mediastinal disorders		
CHRONIC OBSTRUCTIVE PULMONARY DISEASE [A] †	1/359 (0.28%)	1/359 (0.28%)
DYSPNOEA [A] †	0/359 (0%)	1/359 (0.28%)
Surgical and medical procedures		
SURGICAL AND MEDICAL PROCEDURES CARDIOVERSION Systematic Assessment 0 359 1 359 [A] †	1/359 (0.28%)	0/359 (0%)
Vascular disorders		
AORTIC ANEURYSM [A] †	1/359 (0.28%)	0/359 (0%)
AORTIC ARTERIOSCLEROSIS [A] †	0/359 (0%)	1/359 (0.28%)
CIRCULATORY COLLAPSE [A] †	0/359 (0%)	1/359 (0.28%)
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE [A] †	1/359 (0.28%)	0/359 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 2%

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Total	130/359 (36.21%)	129/359 (35.93%)
Ear and labyrinth disorders		
VERTIGO [A] †	9/359 (2.51%)	0/359 (0%)
Gastrointestinal disorders		
CONSTIPATION [A] †	4/359 (1.11%)	10/359 (2.79%)

	Saxagliptin 5 mg	Glimepiride 1 - 6 mg
	Affected/At Risk (%)	Affected/At Risk (%)
DIARRHOEA [A] †	15/359 (4.18%)	19/359 (5.29%)
NAUSEA [A] †	4/359 (1.11%)	8/359 (2.23%)
Infections and infestations		
BRONCHITIS [A] †	14/359 (3.9%)	7/359 (1.95%)
NASOPHARYNGITIS [A] †	23/359 (6.41%)	35/359 (9.75%)
UPPER RESPIRATORY TRACT INFECTION [A] †	12/359 (3.34%)	14/359 (3.9%)
URINARY TRACT INFECTION [A] †	11/359 (3.06%)	18/359 (5.01%)
Injury, poisoning and procedural complications		
CONTUSION [A] †	8/359 (2.23%)	0/359 (0%)
Musculoskeletal and connective tissue disorders		
ARTHRALGIA [A] †	17/359 (4.74%)	9/359 (2.51%)
BACK PAIN [A] †	9/359 (2.51%)	18/359 (5.01%)
MUSCULOSKELETAL PAIN [A] †	9/359 (2.51%)	3/359 (0.84%)
PAIN IN EXTREMITY [A] †	10/359 (2.79%)	9/359 (2.51%)
Nervous system disorders		
DIZZINESS [A] †	6/359 (1.67%)	17/359 (4.74%)
HEADACHE [A] †	6/359 (1.67%)	12/359 (3.34%)
TREMOR [A] †	1/359 (0.28%)	8/359 (2.23%)
Respiratory, thoracic and mediastinal disorders		
COUGH [A] †	9/359 (2.51%)	13/359 (3.62%)
Vascular disorders		
HYPERTENSION [A] †	8/359 (2.23%)	12/359 (3.34%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA 15.0

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.

No publication or presentation may include any of AZ’s confidential information without AZ’s prior written approval.

Results Point of Contact:

Name/Official Title: Boaz Hirshberg , MSD
Organization: AstraZeneca
Phone:
Email: ClinicalTrialTransparency@astrazeneca.com