ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 03/20/2012

ClinicalTrials.gov ID: NCT00575588

Study Identification

Unique Protocol ID:	D1680C00001
Brief Title:	52-week add-on to Metformin Comparison of Saxagliptin and Sulphonylurea, With a 52-week Extension Period
Official Title:	A 52-Week International, Multi-centre, Randomized, Parallel-group, Double-blind, Active-controlled, Phase III Study With a 52-Week Extension Period to Evaluate the Safety and Efficacy of Saxagliptin in Combination With Metformin Compared With Sulphonylurea in Combination With Metformin in Adult Patients With Type 2 Diabetes Who Have Inadequate Glycaemic Control on Metformin Therapy Alone.
Secondary IDs:	EudraCT number 2007-003998-55

Study Status

Record Verification:	March 2012
Overall Status:	Completed
Study Start:	December 2007
Primary Completion:	August 2009 [Actual]
Study Completion:	August 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: 07/H0301/86 Board Name: Essex 1 Research Ethics Committee Board Affiliation: Harlow Essex Phone: 44 01279694917 Email: liz.wrighton@eoe.nhs.uk
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	United Kingdom: Medicines and Healthcare Products Regulatory Agency

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 sulphonylurea in addition with metformin.
Detailed Description:	

Conditions

Conditions:	Type 2 Diabetes
Keywords:	DPP-4 Inhibitors HbA1c incretins

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:	891 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Saxagliptin	Drug: Metformin open-label metformin Drug: Saxagliptin Saxagliptin 5 mg tablets Other Names: • Onglyza
Experimental: Glipizide	Drug: Metformin open-label metformin Drug: Sulphonylurea Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks)

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 prior to Visit 1,
- HbA1c >6.5% and ≤10.0%

Exclusion Criteria:

- Type 1 diabetes,
- history of diabetic ketoacidosis or hyperosmolar non-ketonic coma,
- Insulin therapy within one year of enrolment (with the exception of insulin therapy during a hospitalization or use in gestational diabetes)

Contacts/Locations

Study Officials: Burkhard Goke
Study Principal Investigator
University of Munich, Germany

Peter Ohman, MD
Study Director
AstraZeneca

Deborah Price, MSc
Study Chair
AstraZeneca

Locations: Finland
Research Site
Hanko, Finland

Research Site
Helsinki, Finland

Research Site
Kuopio, Finland

Research Site
Kuusankoski, Finland

Research Site
Mikkeli, Finland

Research Site
Oulu, Finland

Research Site
Tampere, Finland

Germany
Research Site

Aschaffenburg, Germany

Research Site
Berlin, Germany

Research Site
Dortmund, Germany

Research Site
Frankfurt, Germany

Research Site
Hamburg, Germany

Research Site
Hannover, Germany

Research Site
Mainz, Germany

Research Site
Mannheim, Germany

Research Site
Mulheim, Germany

Research Site
Pirna, Germany

Research Site
Ratzeburg, Germany

Research Site
Reinfeld, Germany

Research Site
Rhaunen, Germany

Research Site
Schmiedeberg, Germany

Research Site
Tubingen, Germany

Research Site
Wahlstedt, Germany

Research Site
Weinheim, Germany

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

Research Site
Blackpool, United Kingdom

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

Research Site
Coatbridge, United Kingdom

Research Site
Coventry, United Kingdom

Research Site
Crawley, West Sussex, United Kingdom

Research Site
Glasgow, United Kingdom

Research Site
Hamilton, Lanarkshire, United Kingdom

Research Site
Newcastle, United Kingdom

Research Site
Salford, Manchester, United Kingdom

Research Site
Sheffield, United Kingdom

Research Site
Whitstable, Kent, United Kingdom

Research Site
Motherwell, United Kingdom

Hungary
Research Site
Balatonfured, Hungary

Research Site
Bekescsaba, Hungary

Research Site
Budapest, Hungary

Research Site
Debrecen, Hungary

Research Site
Gyula, Hungary

Research Site
Kalocsa, Hungary

Research Site
Kaposvar, Hungary

Research Site
Kecskemet, Hungary

Research Site
Miskolc, Hungary

Research Site
Mosonmagyarovar, Hungary

Research Site
Nyiregyhaza, Hungary

Research Site
Szekesfehervar, Hungary

India
Research Site
Bangalore, Karnataka, India

Research Site
Indore, Madhya Pradesh, India

Research Site
Jaipur, Rajasthan, India

Research Site
Mumbai, Mashatra, India

Netherlands
Research Site
Beek En Donk, Netherlands

Research Site
Den Bosch, Netherlands

Research Site
Den Haag, Netherlands

Research Site
Deurne, Netherlands

Research Site
Dordrecht, Netherlands

Research Site
Losser, Netherlands

Research Site
Nijverdal, Netherlands

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Rijswijk, Netherlands

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Roelofarendsveen, Netherlands

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Rotterdam, Netherlands

Research Site
Volendam, Netherlands

Norway
Research Site
Bergen, Norway

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Elverum, Norway

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Flatasen, Norway

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Hamar, Norway

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Honefoss, Norway

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Inderoy, Norway

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Oslo, Norway

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Radal, Norway

Research Site
Skedsmokorset, Norway

Research Site
Sogndal, Norway

Research Site
Spikkestad, Norway

Research Site
Trollasen, Norway

Korea, Republic of
Research Site
Guri, Gyeonggi-do, Korea, Republic of

Research Site
Incheon, Korea, Republic of

Research Site
Seongnam, Gyeonggi-do, Korea, Republic of

Research Site
Seoul, Korea, Republic of

Research Site
Uijeongbu-si, Korea, Republic of

Research Site
Wonju, Kangwon-do, Korea, Republic of

Russian Federation
Research Site
Kazan, Russian Federation

Research Site
Moscow, Russian Federation

Research Site
Nizhnii Novgorod, Russian Federation

Research Site
St. Petersburg, Russian Federation

Research Site
Yaroslavl, Russian Federation

Slovakia
Research Site
Dolny Kubin, Slovakia

Research Site
Kosice - Tahanovce, Slovakia

Research Site
Moldava Nad Bodvou, Slovakia

Research Site
Ruzomberok, Slovakia

Research Site
Trnava, Slovakia

Research Site
Zilina, Slovakia

Vietnam
Research Site
Ho Chi Minh, Vietnam

Research Site
Ho Chi Minh City, Vietnam

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	891 participants were enrolled in the study; 33 participants did not enter the treatment period; 858 participants were randomized and treated.

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Overall Study

	Saxagliptin + Metformin	Glipizide + Metformin
Started	428 [1]	430 [1]
Completed	165 [2]	147 [2]
Not Completed	263	283
Adverse Event	11	13
Withdrawal by Subject	27	31
Lost to Follow-up	1	3
Death	4	2
Incorrect enrollment	8	4
Study specific discontinuation criteria	203	218
Severe non-compliance to protocol	5	7
Safety reasons	2	1
Elevated triglyceride	1	0
Patient moved	1	3
Impossible to determine HbA1c	0	1

[1] Randomized and treated

[2] Completed 104 weeks of treatment

Baseline Characteristics

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Baseline Measures

	Saxagliptin + Metformin	Glipizide + Metformin	Total
Number of Participants	428	430	858
Age, Continuous [units: years] Mean (Standard Deviation)	57.50 (10.26)	57.59 (10.37)	57.55 (10.31)
Gender, Male/Female [units: Participants]			
Female	216	198	414
Male	212	232	444

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Hemoglobin A1c (HbA1c) Change From Baseline to Week 52
Measure Description	Adjusted mean change from baseline in HbA1c achieved with saxagliptin added on to metformin versus glipizide added on to metformin at Week 52 (Per Protocol Analysis Set). HbA1c is a continuous measure, the change from baseline for each participant is calculated as the Week 52 value minus the baseline value.
Time Frame	Baseline to 52 Weeks
Safety Issue?	No

Analysis Population Description

Randomized participants who completed the 52 weeks of treatment had both baseline and week 52 HbA1c measurement and had no significant protocol deviations

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Measured Values

	Saxagliptin + Metformin	Glipizide + Metformin
Number of Participants Analyzed	293	293
Hemoglobin A1c (HbA1c) Change From Baseline to Week 52 [units: Percent] Mean (Standard Error)		
Baseline	7.46 (0.045)	7.53 (0.045)
Week 52	6.74 (0.042)	6.71 (0.042)
Adjusted Change from Baseline to Week 52	-0.74 (0.038)	-0.80 (0.038)

Statistical Analysis 1 for Hemoglobin A1c (HbA1c) Change From Baseline to Week 52

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

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	0.06
	Confidence Interval	(2-Sided) 95% -0.05 to 0.16
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.053
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Proportion of Participants Reporting at Least One Episode of Any Hypoglycaemic Event Over 52 Weeks
Measure Description	Proportion of participants reporting at least one episode of any hypoglycaemic event for saxagliptin added on to metformin versus glipizide added on to metformin over 52 weeks (Safety Analysis Set)
Time Frame	From Baseline to Week 52
Safety Issue?	Yes

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Measured Values

	Saxagliptin + Metformin	Glipizide + Metformin
Number of Participants Analyzed	428	430
Proportion of Participants Reporting at Least One Episode of Any Hypoglycaemic Event Over 52 Weeks [units: Percentage of Participants]	3	36.3

Statistical Analysis 1 for Proportion of Participants Reporting at Least One Episode of Any Hypoglycaemic Event Over 52 Weeks

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

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	Between group comparison significant after controlling overall alpha of the study
	Method	Fisher Exact
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-33.2
	Confidence Interval	(2-Sided) 95% -38.1 to -28.5
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Body Weight Change From Baseline to Week 52
Measure Description	Adjusted mean change from baseline in Body Weight achieved with saxagliptin added on to metformin versus glipizide added on to metformin at Week 52 (Safety Analysis Set). Body Weight is a continuous measure, the change from baseline for each participant is calculated as the Week 52 (LOCF) value minus the baseline value.
Time Frame	Baseline, Week 52 (Last Observation Carried Forward)
Safety Issue?	Yes

Analysis Population Description

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

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Measured Values

	Saxagliptin + Metformin	Glipizide + Metformin
Number of Participants Analyzed	424	426
Body Weight Change From Baseline to Week 52 [units: kilogram] Mean (Standard Error)		
Baseline	88.7 (0.91)	88.6 (0.95)
Week 52	87.6 (0.90)	89.7 (0.99)
Adjusted Change from Baseline to Week 52	-1.1 (0.17)	1.1 (0.17)

Statistical Analysis 1 for Body Weight Change From Baseline to Week 52

Statistical Analysis Overview	Comparison Groups	Saxagliptin + Metformin, Glipizide + Metformin
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	Between group comparison significant after controlling overall alpha of the study
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-2.2
	Confidence Interval	(2-Sided) 95% -2.7 to -1.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.24
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Mean Slope of the Regressions of Change From Week 24 to Week 52 in HbA1c
Measure Description	Mean slopes of regression of change from Week 24 to Week 52 in HbA1c for saxagliptin added on to metformin versus glipizide added on to metformin (Per Protocol Analysis Set) achieved by fitting a mixed model with subject specific slopes for the time effect (weeks on randomized treatment was utilized). This analysis gives an assessment of the durability of the HbA1c effect.
Time Frame	Week 24 to Week 52
Safety Issue?	No

Analysis Population Description

Randomized participants who completed the 52 weeks of treatment had both baseline and week 52 HbA1c measurement and had no significant protocol deviations

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Measured Values

	Saxagliptin + Metformin	Glipizide + Metformin
Number of Participants Analyzed	289	293
Mean Slope of the Regressions of Change From Week 24 to Week 52 in HbA1c [units: Percent] Mean (Standard Error)	0.001 (0.001)	0.004 (0.001)

Statistical Analysis 1 for Mean Slope of the Regressions of Change From Week 24 to Week 52 in HbA1c

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

Statistical Test of Hypothesis	P-Value	0.040
	Comments	Between group comparison significant after controlling overall alpha of the study
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.002
	Confidence Interval	(2-Sided) 95% -0.0046 to -0.0001
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.001
	Estimation Comments	[Not specified]

5. Other Pre-specified Outcome Measure:

Measure Title	Hemoglobin A1c (HbA1c) Change From Baseline to Week 104
Measure Description	Adjusted mean change from baseline in HbA1c achieved with saxagliptin added on to metformin versus glipizide added on to metformin at Week 104 (Full Analysis Set). HbA1c is a continuous measure, the change from baseline for each participant is calculated as the Week 104 value minus the baseline value.
Time Frame	Baseline, Week 104
Safety Issue?	No

Analysis Population Description

Number of subjects with observed values at Week 104 was n=184 for saxagliptin + metformin and n=160 for glipizide + metformin

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Measured Values

	Saxagliptin + Metformin	Glipizide + Metformin
Number of Participants Analyzed	423	423
Hemoglobin A1c (HbA1c) Change From Baseline to Week 104 [units: Percent] Mean (Standard Error)		
Baseline	7.65 (0.044)	7.65 (0.041)
Week 104	7.27 (0.050)	7.27 (0.046)
Adjusted Change from Baseline to Week 104	-0.41 (0.041)	-0.35 (0.043)

Statistical Analysis 1 for Hemoglobin A1c (HbA1c) Change From Baseline to Week 104

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

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	
	Comments	[Not specified]
	Method	Other [Repeated Measures]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.05
	Confidence Interval	(2-Sided) 95% -0.17 to 0.06
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.059
	Estimation Comments	[Not specified]

6. Other Pre-specified Outcome Measure:

Measure Title	Proportion of Participants Reporting at Least One Episode of Any Hypoglycaemic Event Over 104 Weeks
Measure Description	Proportion of participants reporting at least one episode of any hypoglycaemic event for saxagliptin added on to metformin versus glipizide added on to metformin over 104 weeks (Safety Analysis Set)
Time Frame	Baseline, Week 104
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Measured Values

	Saxagliptin + Metformin	Glipizide + Metformin
Number of Participants Analyzed	428	430

	Saxagliptin + Metformin	Glipizide + Metformin
Proportion of Participants Reporting at Least One Episode of Any Hypoglycaemic Event Over 104 Weeks [units: Percentage of Participants]	3.5	38.4

Statistical Analysis 1 for Proportion of Participants Reporting at Least One Episode of Any Hypoglycaemic Event Over 104 Weeks

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

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-34.9
	Confidence Interval	(2-Sided) 95% -39.8 to -30.0
	Estimation Comments	[Not specified]

7. Other Pre-specified Outcome Measure:

Measure Title	Body Weight Change From Baseline to Week 104
Measure Description	Adjusted mean change from baseline in Body Weight achieved with saxagliptin added on to metformin versus glipizide added on to metformin at Week 104. Body Weight is a continuous measure, the change from baseline for each participant is calculated as the Week 104 value minus the baseline value.
Time Frame	Baseline, Week 104
Safety Issue?	Yes

Analysis Population Description

Number of subjects with observed values at Week 104 was n=186 for saxagliptin + metformin and n=165 for glipizide + metformin

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin

	Description
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Measured Values

	Saxagliptin + Metformin	Glipizide + Metformin
Number of Participants Analyzed	424	426
Body Weight Change From Baseline to Week 104 [units: kilograms] Mean (Standard Error)		
Baseline	88.69 (0.905)	88.57 (0.955)
Week 104	87.47 (0.898)	89.80 (0.987)
Adjusted Change from Baseline to Week 104	-1.47 (0.200)	1.29 (0.205)

Statistical Analysis 1 for Body Weight Change From Baseline to Week 104

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

Statistical Test of Hypothesis	P-Value	
	Comments	[Not specified]
	Method	Other [Repeated Measures]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-2.76
	Confidence Interval	(2-Sided) 95% -3.32 to -2.20
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.286

	Estimation Comments	[Not specified]

8. Other Pre-specified Outcome Measure:

Measure Title	Mean Slope of the Regressions of Change From Week 24 to Week 104 in HbA1c
Measure Description	Mean slopes of regression of change from Week 24 to Week 104 in HbA1c for saxagliptin added on to metformin versus glipizide added on to metformin (Full Analysis Set) achieved by fitting a mixed model with subject specific slopes for the time effect (weeks on randomized treatment was utilized). This analysis gives an assessment of the durability of the HbA1c effect.
Time Frame	Week 24 to Week 104
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Measured Values

	Saxagliptin + Metformin	Glipizide + Metformin
Number of Participants Analyzed	373	377
Mean Slope of the Regressions of Change From Week 24 to Week 104 in HbA1c [units: Percent] Mean (Standard Error)	0.0041 (0.0005)	0.0076 (0.0005)

Statistical Analysis 1 for Mean Slope of the Regressions of Change From Week 24 to Week 104 in HbA1c

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

Statistical Test of Hypothesis	P-Value	
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.0035
	Confidence Interval	(2-Sided) 95% -0.0048 to -0.0022
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.0007
	Estimation Comments	[Not specified]

Reported Adverse Events

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

Reporting Groups

	Description
Saxagliptin + Metformin	Saxagliptin 5 mg tablets added on to open-label metformin
Glipizide + Metformin	Glipizide 5-20 mg capsules (titrated to optimal effect or highest tolerable dose during 18 weeks) added on to open-label metformin

Serious Adverse Events

	Saxagliptin + Metformin	Glipizide + Metformin
	Affected/At Risk (%)	Affected/At Risk (%)
Total	54/428 (12.62%)	55/430 (12.79%)
Cardiac disorders		
Angina Pectoris [A] †	1/428 (0.23%)	0/430 (0%)
Angina Unstable [A] †	0/428 (0%)	2/430 (0.47%)

	Saxagliptin + Metformin	Glipizide + Metformin
	Affected/At Risk (%)	Affected/At Risk (%)
Arrhythmia [A] †	1/428 (0.23%)	0/430 (0%)
Arteriosclerosis Coronary Artery [A] †	0/428 (0%)	1/430 (0.23%)
Atrial Fibrillation [A] †	2/428 (0.47%)	2/430 (0.47%)
Atrioventricular Block Complete [A] †	1/428 (0.23%)	0/430 (0%)
Bradycardia [A] †	0/428 (0%)	1/430 (0.23%)
Cardiac Failure [A] †	1/428 (0.23%)	1/430 (0.23%)
Coronary Artery Disease [A] †	2/428 (0.47%)	1/430 (0.23%)
Coronary Artery Occlusion [A] †	0/428 (0%)	1/430 (0.23%)
Coronary Artery Stenosis [A] †	1/428 (0.23%)	0/430 (0%)
Myocardial Infarction [A] †	1/428 (0.23%)	1/430 (0.23%)
Myocardial Ischemia [A] †	1/428 (0.23%)	0/430 (0%)
Supraventricular Tachycardia [A] †	1/428 (0.23%)	0/430 (0%)
Ventricular Fibrillation [A] †	1/428 (0.23%)	0/430 (0%)
Congenital, familial and genetic disorders		
Hydrocele [A] †	1/428 (0.23%)	0/430 (0%)
Ear and labyrinth disorders		
Deafness Bilateral [A] †	1/428 (0.23%)	0/430 (0%)
Vertigo [A] †	0/428 (0%)	1/430 (0.23%)
Endocrine disorders		
Hyperthyroidism [A] †	0/428 (0%)	1/430 (0.23%)
Eye disorders		
Cataract [A] †	2/428 (0.47%)	0/430 (0%)
Retinal Vein Occlusion [A] †	0/428 (0%)	1/430 (0.23%)

	Saxagliptin + Metformin	Glipizide + Metformin
	Affected/At Risk (%)	Affected/At Risk (%)
Gastrointestinal disorders		
Abdominal Pain [A] †	0/428 (0%)	1/430 (0.23%)
Abdominal Pain Upper [A] †	1/428 (0.23%)	0/430 (0%)
Acute Abdomen [A] †	0/428 (0%)	1/430 (0.23%)
Food Poisoning [A] †	1/428 (0.23%)	0/430 (0%)
Gastric Hemorrhage [A] †	0/428 (0%)	1/430 (0.23%)
Gastric Ulcer [A] †	1/428 (0.23%)	0/430 (0%)
Gastroesophageal Reflux Disease [A] †	0/428 (0%)	2/430 (0.47%)
Inguinal Hernia [A] †	1/428 (0.23%)	1/430 (0.23%)
Pancreatitis [A] †	0/428 (0%)	1/430 (0.23%)
Pancreatitis Acute [A] †	0/428 (0%)	1/430 (0.23%)
Rectal Hemorrhage [A] †	1/428 (0.23%)	1/430 (0.23%)
Upper Gastrointestinal Hemorrhage [A] †	1/428 (0.23%)	0/430 (0%)
General disorders		
Chest Pain [A] †	1/428 (0.23%)	1/430 (0.23%)
Device Malfunction [A] †	1/428 (0.23%)	0/430 (0%)
Hepatobiliary disorders		
Biliary Colic [A] †	0/428 (0%)	1/430 (0.23%)
Cholecystitis [A] †	0/428 (0%)	1/430 (0.23%)
Cholecystitis acute [A] †	0/428 (0%)	1/430 (0.23%)
Cholelithiasis [A] †	1/428 (0.23%)	1/430 (0.23%)
Hepatitis [A] †	0/428 (0%)	1/430 (0.23%)
Immune system disorders		

	Saxagliptin + Metformin	Glipizide + Metformin
	Affected/At Risk (%)	Affected/At Risk (%)
Allergy To Arthropod Sting [A] †	1/428 (0.23%)	0/430 (0%)
Hypersensitivity [A] †	1/428 (0.23%)	1/430 (0.23%)
Infections and infestations		
Anal Abscess [A] †	1/428 (0.23%)	0/430 (0%)
Biliary Tract Infection [A] †	0/428 (0%)	1/420 (0.24%)
Helicobacter Gastritis [A] †	0/428 (0%)	1/430 (0.23%)
Herpes Zoster Ophthalmic [A] †	1/428 (0.23%)	0/430 (0%)
Pneumonia [A] †	2/428 (0.47%)	1/430 (0.23%)
Pulmonary Tuberculosis [A] †	1/428 (0.23%)	0/430 (0%)
Pyelonephritis [A] †	1/428 (0.23%)	0/430 (0%)
Salmonella Sepsis [A] †	1/428 (0.23%)	0/430 (0%)
Superinfection [A] †	0/428 (0%)	1/430 (0.23%)
Urosepsis [A] †	1/428 (0.23%)	0/430 (0%)
Injury, poisoning and procedural complications		
Concussion [A] †	0/428 (0%)	1/430 (0.23%)
Contusion [A] †	1/428 (0.23%)	0/430 (0%)
Femoral Neck Fracture [A] †	1/428 (0.23%)	0/430 (0%)
Femur Fracture [A] †	0/428 (0%)	1/430 (0.23%)
Head Injury [A] †	1/428 (0.23%)	0/430 (0%)
Humerus Fracture [A] †	0/428 (0%)	1/430 (0.23%)
Injury [A] †	0/428 (0%)	1/430 (0.23%)
Ligament Rupture [A] †	0/428 (0%)	1/430 (0.23%)

	Saxagliptin + Metformin	Glipizide + Metformin
	Affected/At Risk (%)	Affected/At Risk (%)
Lumbar Vertebral Fracture [A] †	1/428 (0.23%)	0/430 (0%)
Meniscus Lesion [A] †	1/428 (0.23%)	0/430 (0%)
Open Wound [A] †	0/428 (0%)	1/430 (0.23%)
Patella Fracture [A] †	1/428 (0.23%)	0/430 (0%)
Tendon Rupture [A] †	0/428 (0%)	1/430 (0.23%)
Upper Limb Fracture [A] †	1/428 (0.23%)	0/430 (0%)
Metabolism and nutrition disorders		
Diabetes Mellitus [A] †	0/428 (0%)	1/430 (0.23%)
Musculoskeletal and connective tissue disorders		
Arthritis [A] †	1/428 (0.23%)	0/430 (0%)
Arthropathy [A] †	1/428 (0.23%)	0/430 (0%)
Intervertebral Disc Protrusion [A] †	1/428 (0.23%)	0/430 (0%)
Jaw Cyst [A] †	1/428 (0.23%)	0/430 (0%)
Osteoarthritis [A] †	2/428 (0.47%)	1/430 (0.23%)
Osteochondrosis [A] †	1/428 (0.23%)	1/430 (0.23%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Acute Myeloid Leukemia [A] †	1/428 (0.23%)	0/430 (0%)
Bladder Neoplasm [A] †	0/428 (0%)	1/430 (0.23%)
Bladder Cancer [A] †	1/428 (0.23%)	0/430 (0%)
Breast Cancer [A] †	0/428 (0%)	1/430 (0.23%)
Bronchial Carcinoma [A] †	0/428 (0%)	1/430 (0.23%)
Colon Cancer [A] †	2/428 (0.47%)	0/430 (0%)

	Saxagliptin + Metformin	Glipizide + Metformin
	Affected/At Risk (%)	Affected/At Risk (%)
Colon Neoplasm [A] †	0/428 (0%)	1/430 (0.23%)
Lip Neoplasm Malignant Stage Unspecified [A] †	0/428 (0%)	1/430 (0.23%)
Lung Neoplasm malignant [A] †	0/428 (0%)	1/430 (0.23%)
Malignant Melanoma [A] †	0/428 (0%)	1/430 (0.23%)
Metastases to Central Nervous System [A] †	1/428 (0.23%)	0/430 (0%)
Metastasis To Liver [A] †	1/428 (0.23%)	0/430 (0%)
Renal Cancer [A] †	0/428 (0%)	1/430 (0.23%)
Salivary Gland Neoplasm [A] †	1/428 (0.23%)	0/430 (0%)
Thyroid Cancer [A] †	1/428 (0.23%)	0/430 (0%)
Tumor Ulceration [A] †	0/428 (0%)	1/430 (0.23%)
Nervous system disorders		
Cerebral Ischemia [A] †	0/428 (0%)	1/430 (0.23%)
Cerebrovascular Accident [A] †	1/428 (0.23%)	1/430 (0.23%)
Cerebrovascular Disorder [A] †	1/428 (0.23%)	0/430 (0%)
Epilepsy [A] †	1/428 (0.23%)	0/430 (0%)
Headache [A] †	0/428 (0%)	1/430 (0.23%)
Hypertensive Encephalopathy [A] †	1/428 (0.23%)	0/430 (0%)
Ischemic Stroke [A] †	0/428 (0%)	1/430 (0.23%)
Transient Ischemic Attack [A] †	0/428 (0%)	1/430 (0.23%)
Vertebrobasilar Insufficiency [A] †	1/428 (0.23%)	0/430 (0%)
Psychiatric disorders		
Agitation [A] †	0/428 (0%)	1/430 (0.23%)

	Saxagliptin + Metformin	Glipizide + Metformin
	Affected/At Risk (%)	Affected/At Risk (%)
Renal and urinary disorders		
Nephrolithiasis [A] †	1/428 (0.23%)	0/430 (0%)
Renal Failure Acute [A] †	1/428 (0.23%)	0/430 (0%)
Urinary Retention [A] †	0/428 (0%)	1/430 (0.23%)
Reproductive system and breast disorders		
Benign Prostatic Hyperplasia [A] †	0/428 (0%)	1/430 (0.23%)
Endometrial Hyperplasia [A] †	1/428 (0.23%)	0/430 (0%)
Respiratory, thoracic and mediastinal disorders		
Asthma [A] †	1/428 (0.23%)	0/430 (0%)
Bronchitis Chronic [A] †	1/428 (0.23%)	0/430 (0%)
Dyspnea [A] †	0/428 (0%)	1/430 (0.23%)
Laryngeal Edema [A] †	0/428 (0%)	1/430 (0.23%)
Pulmonary Embolism [A] †	0/428 (0%)	1/430 (0.23%)
Vascular disorders		
Aortic Aneurysm [A] †	1/428 (0.23%)	0/430 (0%)
Arteriosclerosis [A] †	0/428 (0%)	1/430 (0.23%)
Circulatory Collapse [A] †	0/428 (0%)	1/430 (0.23%)
Hypertension [A] †	0/428 (0%)	3/430 (0.7%)
Hypertensive Crisis [A] †	0/428 (0%)	3/430 (0.7%)
Hypotension [A] †	0/428 (0%)	1/430 (0.23%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 13.0

Other Adverse Events

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

	Saxagliptin + Metformin	Glipizide + Metformin
	Affected/At Risk (%)	Affected/At Risk (%)
Total	105/428 (24.53%)	201/430 (46.74%)
Gastrointestinal disorders		
Diarrhoea [A] †	25/428 (5.84%)	17/430 (3.95%)
Infections and infestations		
Nasopharyngitis [A] †	46/428 (10.75%)	41/430 (9.53%)
Upper Respiratory Tract Infection [A] †	25/428 (5.84%)	16/430 (3.72%)
Metabolism and nutrition disorders		
Hypoglycaemia [A] †	15/428 (3.5%)	165/430 (38.37%)
Vascular disorders		
Hypertension [A] †	19/428 (4.44%)	27/430 (6.28%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA 13.0

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.

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