Beneficios de la combinación saxagliptin/metformin liberación prolongada

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Conflictos de interés

- Conferencista: Astra Zeneca, Abbott Nutrición, Novartis Oncology, Novo Nordisk, Merck Sharp & Dohme, Roche, Glaxo SmithKline, Sanofi Aventis, Genzyme
- Advisory Board: Novartis Oncology, Sanofi Aventis, Astra Zeneca, Novo Nordisk
- Investigación clínica: Astra Zeneca, Novartis Pharma Logistics Inc., Merck Sharp & Dohme, Glaxo SmithKline, Organon, Boehringer Ingelheim, Roche

Agenda

- Hay diferencias entre inhibidores de DPP-4?
- Saxagliptin/metformin XR, diferencias
- Cuál es la importancia de la formulación?
- Inestabilidad glicémica
- Seguridad cardiovascular y datos en ICC

Inhibidores de DPP-4

- Sitagliptina
- Vildagliptina
- Linagliptina
- Saxagliptina
- Alogliptin

- Hay alguna diferencia entre ellas?

Inhibidores de DPP-4

- Eficacia clínica:
  - No hay estudios comparativos directos
  - Comparaciones indirectas muestran eficacia similar
- Posología:
  - OD: sitagliptina, linagliptina, saxagliptina, alogliptina
  - Bid: vildagliptina
    - Por seguridad hepática en fase II
  - Semanal: omariglitptina

Diferencias cinéticas

- Inhibición del DPP-4
  - No relevante por tener vidas medias largas de inhibición
- Vía de eliminación
  - Renal: sitagliptina, saxagliptina, vildagliptina
    - Reducir dosis 50% si AEC <50 cc/min
  - Hepático: linagliptina
    - No ajuste de dosis en insuficiencia renal
    - La ventaja se pierde en combinación con metformin

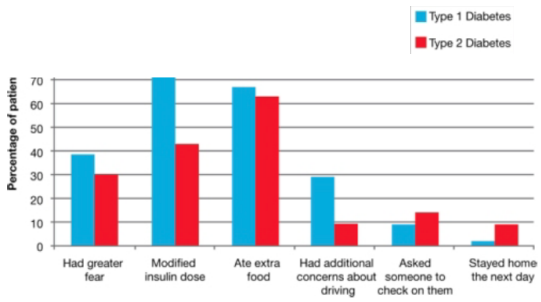
Diferencias cinéticas

- Sustrato de citocromos:
  - CYP3A4: saxagliptina
  - Interacciones con inhibidores o inductores potentes como ketoconazole

Otras diferencias

- Seguridad cardiovascular:
  - Estudios publicados: SAVOR y EXAMINE
  - Todos los demás en curso
- Terapia combinada:
  - Metformin liberación rápida: sitagliptina, vildagliptina, linagliptina
  - Metformin XR: saxagliptina

QUÉ IMPACTO PUEDE PRODUCIR LA HIPOGLICEMIA?



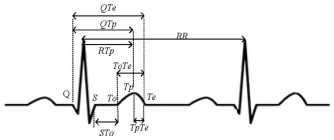
Tenzer-Iglesias. J Fam Prac. 2012;61(10):S1

Otras consecuencias

- Ansiedad
- Depresión
- Uso de recursos de salud
- Costo
- Pobre adherencia a tratamiento
- Accidente automonitriz
- Fracturas

Moghissi E. Endocr Pract. 2013;19(3):526

Cambios ECG en hipoglicemia



ECG parameter	Nonhypoglycemia	Hypoglycemia	*p* value
HR	1.052 ± 0.061	1.197 ± 0.128	<0.0001
QTe_c	1.040 ± 0.031	1.074 ± 0.054	<0.0001
$TpTe_c$	1.031 ± 0.032	1.074 ± 0.071	<0.0001
QTp_c	1.058 ± 0.071	1.106 ± 0.096	<0.005
$ToTe_c$	1.058 ± 0.071	1.106 ± 0.096	<0.005
RTp_c	1.044 ± 0.039	1.068 ± 0.056	<0.01
STo_c	0.994 ± 0.141	0.940 ± 0.193	<0.1

Nuryani N. Annals Biomed Eng. 2012;40:934

Hipoglicemia e isquemia miocárdica

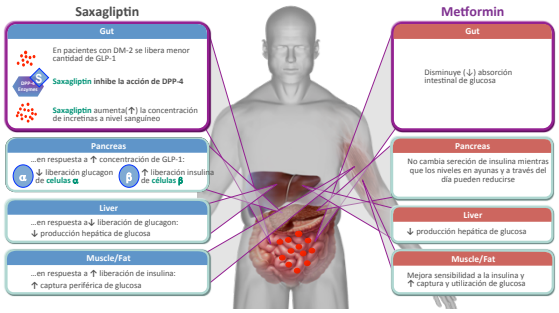
	Total episodes	Episodes with chest pain/ angina	Episodes with ECG abnormalities
Hypoglycemia	54	10*	6*
Symptomatic	26	10*	4*
Asymptomatic	28	—	2
Normoglycemia without rapid changes	N/A	0	0
Hyperglycemia	59	1	0
Rapid changes in glucose (>100 mg · dl^{-1} · h^{-1})	50	9*	2

*$P < 0.01$ vs. episodes during hyperglycemia and normoglycemia.

Desouza C. Diabetes Care. 2003;26:1485

SAXAGLIPTINA/METFORMINA XR

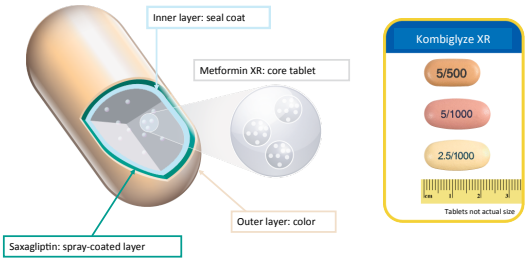
Saxagliptin/metformin XR: mecanismos de acción complementarios



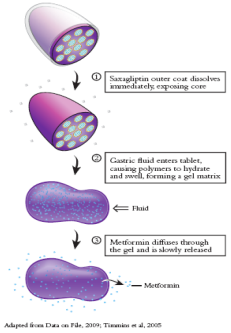
GLP=glucagon-like peptide; DPP=dipeptidyl peptidase.

1. Verspohl EJ. *Pharmacol Ther* 2009;124:113-138.

Saxagliptin y metformin HCl XR: Tabletas de combinación fija



Liberación de saxagliptin y metformin XR



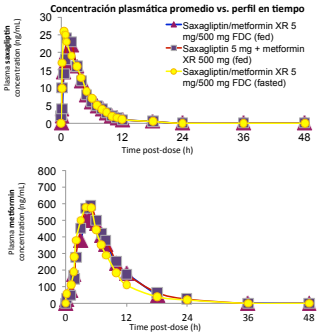
Adapted from Data on File, 2009; Timmins et al, 2005

Saxagliptina/metformin XR

- El programa fase III fue desarrollado con la combinación de saxagliptina/meformin IR
- Equivalencia en niveles séricos y efectos terapéuticos cuando se combina saxagliptina con metfomrin IR ó XR

Saxagliptin/metformin XR es bioequivalente a los componentes individuales saxagliptin y metformin XR

Estos estudios demuestran que en sujetos sanos las tabletas de saxagliptin/metformin XR son bioequivalentes a la coadministración de saxagliptin y metformin XR como tabletas separadas en condiciones bajo alimentación



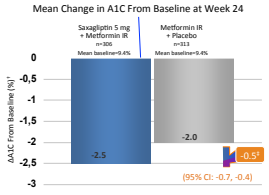
Boulton et al *Clin Drug Investig* 2011; 31 (9)

Saxagliptin + metformin IR vs metformin IR

Pacientes vírgenes de tratamiento

Tratamiento de primera línea

Treatment-Naive: A1C*



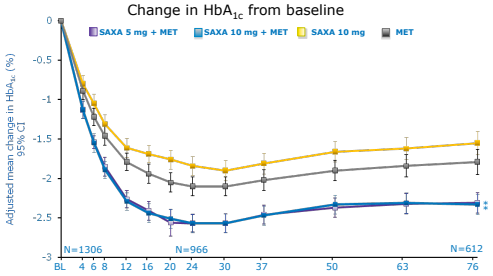
- Mean daily metformin IR doses at Week 24 were 1790 mg for saxagliptin 5 mg + metformin IR and 1817 mg for metformin IR + placebo[1]
- The proportion of patients discontinued or rescued for metformin IR alone, saxagliptin 10 mg, saxagliptin 5 mg + metformin IR, and saxagliptin 10 mg + metformin IR was 10.1%, 21.2%, 7.5%, and 5.9%, respectively[1]
- Incidence of reported hypoglycemia§ was 3.4% in treatment-naive patients given saxagliptin 5 mg + metformin IR and 4.0% in patients given metformin IR + placebo
- Adverse reactions with saxagliptin 5 mg + metformin IR reported in ≥5% of patients and more commonly than in patients treated with metformin IR + placebo were headache (7.5% vs 5.2%) and nasopharyngitis (6.9% vs 4.0%)

* Intent-to-treat population using last observation on study, or last observation prior to pioglitazone rescue therapy for patients needing rescue.
† Least squares mean adjusted for baseline value.
‡ $P<0.0001$ compared to metformin IR + placebo.
§ A concurrent glucose measurement was not required or was normal in some patients. Therefore, it is not possible to conclusively determine that all these reports reflected true hypoglycemia.
IR=immediate release; CI=confidence interval.

1. Jadzinsky M et al. *Diabetes Obes Metab* 2009;11:611-622.

Initial combination with metformin: 76-week extension

Change in HbA_{1c} from baseline



*Post hoc p<0.0001 vs both SAXA 10 mg and MET alone.
MET: metformin; SAXA: saxagliptin.

Pfützner , A. et al. *Diabetes, Obesity and Metabolism* 13: 567–576, 2011

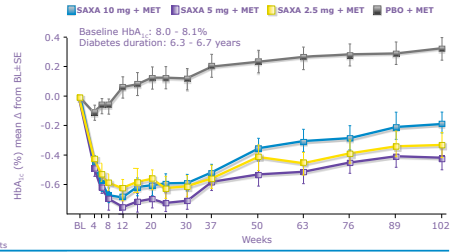
Saxagliptin + metformin IR vs placebo + metformin IR

Pacientes no controlados con metformin

Segunda línea de tratamiento

Saxagliptin agregado a metformin: extensión de 102-semanas

Cambio promedio HbA1c desde basal

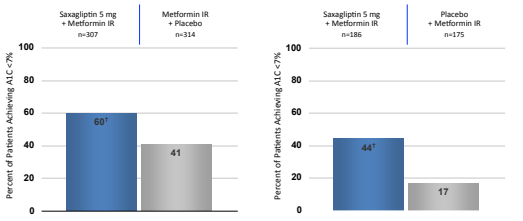


Patients								
SAXA 2.5 mg + MET	192	152	117	105	96	79	67	21
SAXA 5 mg + MET	191	146	116	99	89	70	58	25
SAXA 10 mg + MET	181	140	124	111	93	80	68	32
PBO + MET	179	111	72	60	52	33	25	15

BL: Baseline; MET: Metformin; PBO: Placebo; SAXA: Saxagliptin.

Ravichandran S, et al. *Diabetologia* 2009; 52(Suppl. 1):S60 [Abstract]. Presented as an Oral Presentation at the European Association for the Study of Diabetes Congress, Vienna, Austria, September 2009 [Presentation no. 132]

Pacientes que alcanzan A1C <7% a la semana 24



- Patients achieving A1C <7% with saxagliptin 2.5 mg, 5 mg, 10 mg + metformin IR was 37%, 44% and 44% vs 17 % placebo + metformin IR ; *P* <0.0001 at Week 24.

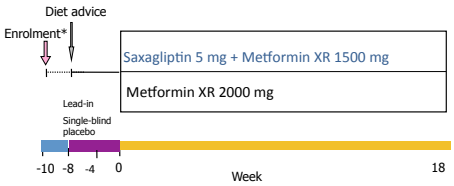
* Intent-to-treat population using last observation on study, or last observation prior to pioglitazone rescue therapy for patients needing rescue.
† *P*<0.05 compared to placebo + metformin IR.
IR=immediate release.

1. Jadzinsky M et al. *Diabetes Obes Metab*. 2009;11:611-622.
2. DeFronzo RA et al. *Diabetes Care*. 2009;32(9):1649-1655.

Saxagliptin + Metformin XR

Comparado con aumento de dosis de Metformin XR

Saxagliptin + Metformin XR vs. Metformin XR Uptitration

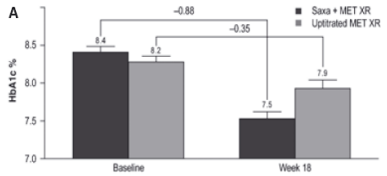


* Patients with type 2 diabetes with inadequate glycemic control defined as HbA1c >6.5 % and ≤10.5% (at randomization), on a stable dose (≥850 mg and ≤1500mg) of metformin IR or XR therapy for at least 8 weeks will enter an 8 week lead-in period. Patients on a stable dose (1500mg) of metformin XR will enter a 4 week lead-in period.

Fonseca, V et al *Diabetes, Obesity and Metabolism* 14: 365–371, 2012.

Saxagliptin + Metformin XR vs. aumento de dosis de metformin XR

Mean HbA1c at baseline and week 18

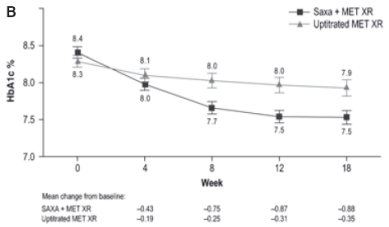


Adjusted mean change from baseline HbA1c, was −0.88% for saxagliptin + metformin XR and −0.35% for uptitrated metformin XR; the between-group difference was−0.52% (p < *0.0001)*

Fonseca, V et al *Diabetes, Obesity and Metabolism* 14: 365–371, 2012.

Saxagliptin + Metformin XR vs. aumento de dosis metformin XR

Mean change in HbA1c over 18 weeks of treatment (LOCF)



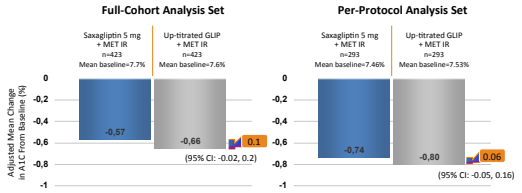
From week 8 through week 18, decreases in mean HbA1c were greater in patients receiving saxagliptin + metformin XR than in those receiving uptitrated metformin XR

Fonseca, V et al *Diabetes, Obesity and Metabolism* 14: 365–371, 2012.

Saxagliptin + Metformin IR

Comparado con GLIPIZIDE + Metformin IR

A1C at Week 52[1]

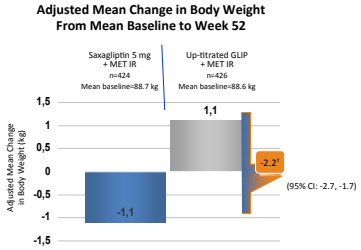


- The upper limit of this 95% CI met the predefined criterion for non-inferiority of <0.35%. Thus, saxagliptin 5 mg + MET IR was non-inferior to up-titrated GLIP + MET IR
- A conclusion of non-inferiority of saxagliptin to up-titrated GLIP may be limited to patients with baseline A1C comparable to those in the trial (91% of patients had baseline A1C <9%)
- Mean final GLIP dose in the titrated arm was 14.7 mg/day; 50% of patients received 20 mg/day
- The proportion of patients who discontinued due to lack of efficacy by Week 52 in the saxagliptin + MET IR group and the up-titrated GLIP + MET IR group was 15.3% and 12.0%, respectively[2]

MET IR=metformin immediate release; GLIP=glipizide; CI=confidence interval.

1. Göke B et al. *Int J Clin Pract*. 2010;64(12):1619-1631.
2. Data on file, SAXA 070. Bristol-Myers Squibb Company. Princeton, NJ.

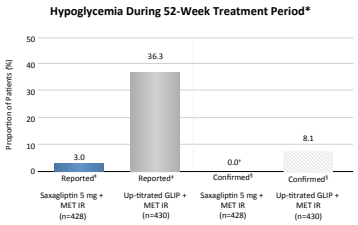
Add-On to MET IR Versus GLIP + MET IR: Body Weight*



* Safety analysis set.
† *P*<0.0001 vs up-titrated GLIP + MET IR.
MET IR=metformin immediate release; GLIP=glipizide; CI=confidence interval.

Göke B et al. *Int J Clin Pract* 2010;64(12):1619-1631.

Add-On to MET IR Versus GLIP + MET IR: Hypoglycemia



Reported Hypoglycemia:

- **13 patients in the saxagliptin 5 mg + MET IR group reported 19 hypoglycemic events**
- **156 patients in the up-titrated GLIP + MET IR group reported 750 hypoglycemic events**

‡ Reported hypoglycemia events were a combination of reports of either signs or symptoms consistent with hypoglycemia with or without documented glucose levels or reported low glucose levels without any symptoms. Therefore, it is not possible to conclusively determine that all these reports reflected true hypoglycemia.

§ Confirmed hypoglycemia was defined as a fingerstick glucose ≤50 mg/dL with associated symptoms.

* Safety analysis set.
† *P*<0.0001 vs up-titrated GLIP + MET IR group.
‡ MET IR=metformin immediate release; GLIP=glipizide.

Göke B et al. *Int J Clin Pract* 2010;64(12):1619-1631.

Saxagliptin + Metformin IR + Insulin

Vs Placebo + Metformin + Insulin

Tratamiento de tercera línea

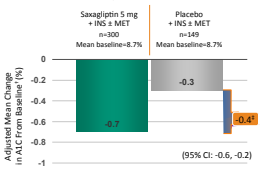
Demographic and Baseline Characteristics (cont)

Characteristic	Saxagliptin 5 mg + INS (n=304)	MET IR + Placebo (n=151)
MTDDI, units (range)	53.6 (19–150)	55.3 (30–149)
Insulin type, n (%)		
No premixed	115 (38)	69 (46)
Intermediate acting and long acting	9 (3)	8 (5)
Intermediate acting, alone	54 (18)	32 (21)
Long-acting, alone	52 (17)	29 (19)
Any premixed	189 (62)	82 (54)
Premixed alone	182 (60)	76 (50)
Intermediate acting and premixed	4 (1)	4 (3)
Long acting and premixed	3 (1)	2 (1)
Patients taking MET, n (%)	209 (69)	105 (70)
MET dose, mean (range), mg	1805.4 (250–3000)	1861.1 (850–3000)

INS=insulin; MET=metformin; IR=immediate release; MTDDI=mean total daily dose of insulin.

Barnett AH, et al. *Curr Med Res Opin* 2012. doi:10.1185/03007995.2012.665046.

Change in A1C at Week 24*



- Similar mean reductions in A1C versus placebo were observed for patients treated with saxagliptin 5 mg + INS alone and saxagliptin 5 mg + INS ± MET (-0.4% and -0.4%, respectively)
- The proportion of patients who discontinued for lack of glycemic control or who were rescued for meeting prespecified glycemic criteria in the saxagliptin 5 mg + INS ± MET group and the placebo + INS ± MET group was 23% and 32%, respectively

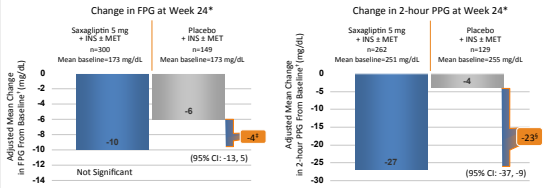
* Intent-to-treat population using last observation on study or last observation prior to INS rescue therapy for patients needing rescue.

† Least squares mean adjusted for baseline value and MET use at baseline.

‡ P<0.0001 compared to placebo + INS ± MET.

INS=insulin; MET=metformin; CI=confidence interval.

Barnett AH, et al. *Curr Med Res Opin* 2012. doi:10.1185/03007995.2012.665046.



- * Intent-to-treat population using last observation on study or last observation prior to INS rescue therapy for patients needing rescue.
- † Least squares mean adjusted for baseline value and MET use at baseline.
- ‡ Difference compared to placebo + INS ± MET was not statistically significant.
- § $P<0.05$ compared to placebo + INS ± MET.

INS=insulin; MET=metformin; FPG=fasting plasma glucose; PPG=postprandial glucose; CI=confidence interval.

Barnett AH, et al. *Curr Med Res Opin* 2012. doi:10.1185/03007995.2012.665046.

INESTABILIDAD GLICÉMICA

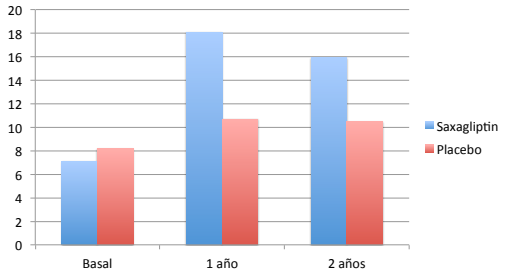
Saxagliptin Assessment of Vascular Outcomes Recorded in Patients With Diabetes Mellitus–Thrombolysis in Myocardial Infarction (SAVOR-TIMI) 53 Study

Bristol-Myers Squibb AstraZeneca

Inestabilidad glicémica

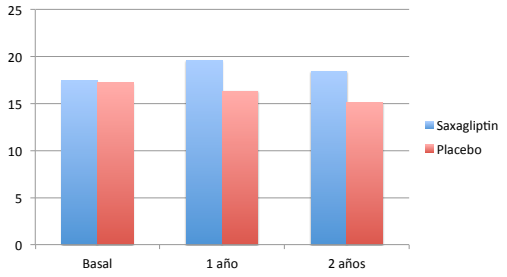
- Necesidad de agregar otro antidiabético por más de 3 meses
- Aumento de dosis de insulina >25% por más de 3 meses
- Necesidad de inicio de insulina por más de 3 meses
- Aumento de Hba1c >0.5% después de la aleatorización

SAVOR: pacientes con hba1c <6.5%



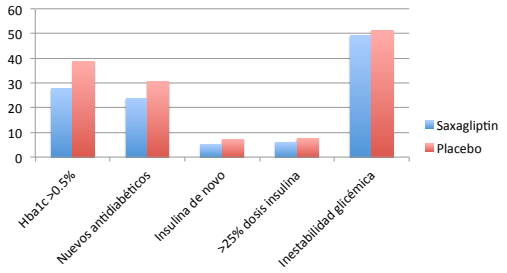
Leibowitz G. Diab Obes Metab. 2015, early on line.

SAVOR: pacientes con hba1c 6.5-7%



Leibowitz G. Diab Obes Metab. 2015, early on line.

SAVOR: pacientes inestabilidad glicémica



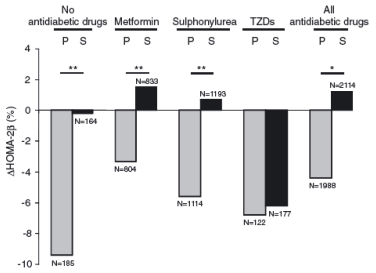
Leibowitz G. Diab Obes Metab. 2015, early on line.

Factores predictores de inestabilidad glicémica

- Origen asiático
- Edad más joven al diagnóstico
- Mayor duración de DM
- Tabaquismo
- Niveles altos de Hba1c
- Niveles mayores de AEC calculado
- Nivel bajo de HDL
- Tratamiento de base con SU o TZD

Leibowitz G. Diab Obes Metab. 2015, early on line.

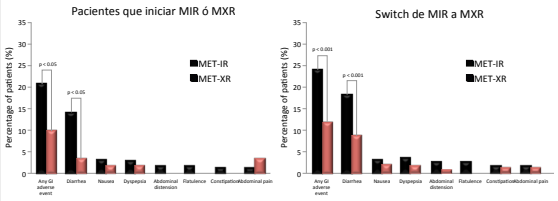
HOMA beta



Leibowitz G. Diab Obes Metab. 2015, early on line.

Seguridad y tolerabilidad

Tolerabilidad de metformin XR y metformin IR



Patients who were initiated on MET-XR or who were switched from MIR to MXR experienced fewer GI adverse events on comparable doses of metformin

GI, gastrointestinal; MET, metformin; MET-IR, immediate-release metformin; MET-XR, extended-release metformin.

Blonde L, *et al. Curr Med Res Opin* 2004;20:565–72.

Gastrointestinal Adverse Events in ≥5% Patients Treated With Saxagliptin and Metformin IR

- In patients treated with the combination of saxagliptin and metformin IR, either in treatment-naive patients or in patients uncontrolled on metformin monotherapy, diarrhea was the only gastrointestinal-related event that occurred in ≥5% in any treatment group across both studies

Treatment-Naive[1]		
	Patients (%)	
	Saxagliptin 5 mg + Metformin IR (n=320)	Metformin IR + Placebo (n=328)
Diarrhea	6.9%	7.3%

Uncontrolled on Metformin Monotherapy[2]			
	Patients (%)		
	Saxagliptin 5 mg + Metformin IR (n=191)	Saxagliptin 2.5 mg + Metformin IR (n=192)	Placebo + Metformin IR (n=179)
Diarrhea	5.8%	9.9%	11.2%

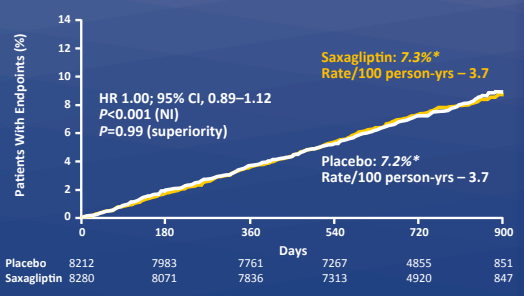
IR=immediate release.

1. Jadzinsky M et al. *Diabetes Obes Metab* 2009;11:611-622.
2. DeFronzo RA et al. *Diabetes Care* 2009;32(9):1649-1655.

SEGURIDAD CARDIOVASCULAR

Saxagliptin Assessment of Vascular Outcomes Recorded in Patients With Diabetes Mellitus–Thrombolysis in Myocardial Infarction (SAVOR-TIMI) 53 Study

Kaplan-Meier Rates of the Primary Composite Endpoint – CV Death, MI, or Stroke



Placebo	8212	7983	7761	7267	4855	851
Saxagliptin	8280	8071	7836	7313	4920	847

*K-M event rates are presented after 2 yrs.
HR: hazard ratio; K-M: Kaplan-Meier; Pbo: placebo; Saxa: saxagliptin
Scirica BM, et al. *N Engl J Med.* 2013.10.1056/NEJMoa1307684.

Individual Components of the Composite Endpoints

Efficacy endpoint	Saxagliptin n (%)* (N = 8,280)	Placebo n (%)* (N = 8,212)	HR (95% CI)	*P* value
CV death	269 (3.2)	260 (2.9)	1.03 (0.87–1.22)	0.72
MI	265 (3.2)	278 (3.4)	0.95 (0.80–1.12)	0.52
Ischemic stroke	157 (1.9)	141 (1.7)	1.11 (0.88–1.39)	0.38
Hosp for UA	97 (1.2)	81 (1.0)	1.19 (0.89–1.60)	0.24
Hosp for HF	289 (3.5)	228 (2.8)	1.27 (1.07–1.51)	0.007
Hosp for coronary revasc.	423 (5.2)	459 (5.6)	0.91 (0.80–1.04)	0.18

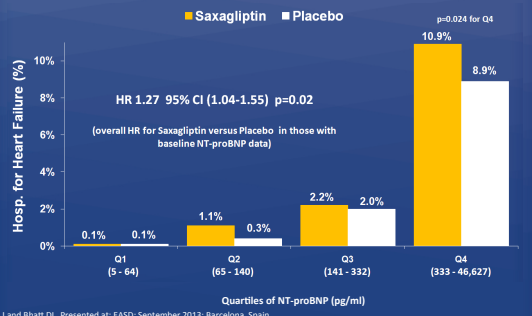
*K-M event rates are presented after 2 yrs.

Scirica BM, et al. *N Engl J Med.* 2013.10.1056/NEJMoa1307684.

Bristol-Myers Squibb AstraZeneca

Baseline NT-pro BNP and Hospitalization for Heart Failure

Preliminary data (N=12,397 patients; 387 HF events)



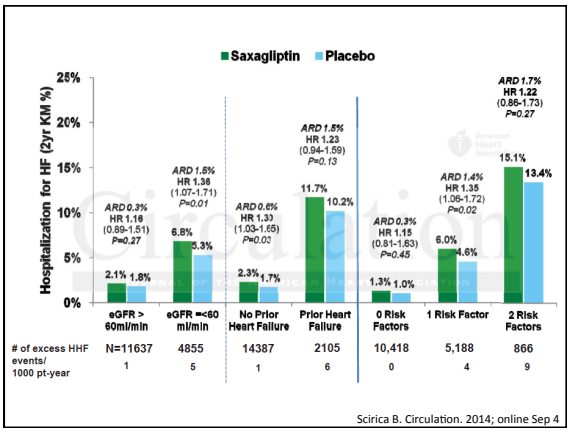
Raz I and Bhatt DL. Presented at: EASD; September 2013; Barcelona, Spain.

Bristol-Myers Squibb AstraZeneca

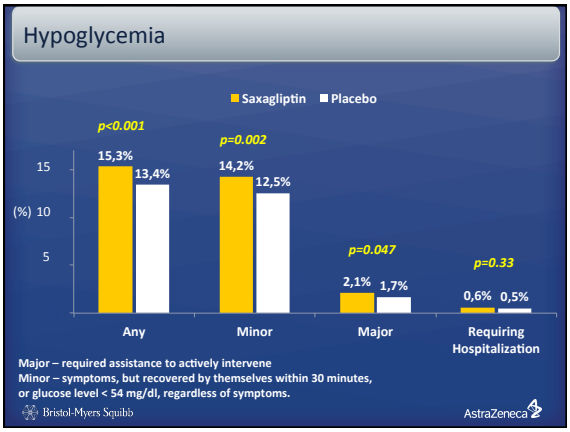
SAVOR e ICC

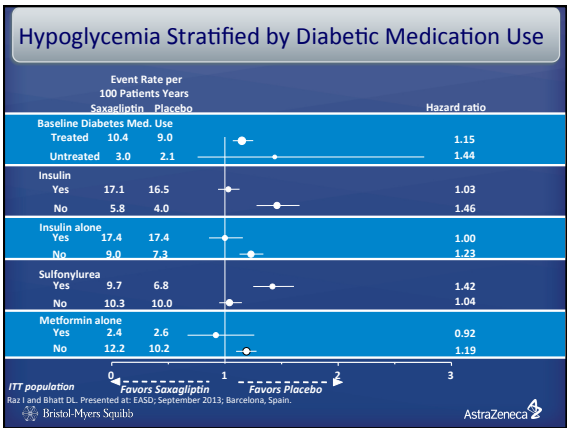
- Factores de riesgo:
  - Historia previa de falla cardíaca
  - AEC <60 cc/min
  - Microalbuminuria

Scirica B. Circulation. 2014; online Sep 4



Scirica B. Circulation. 2014; online Sep 4





ORIGINAL ARTICLE

Alogliptin after Acute Coronary Syndrome in Patients with Type 2 Diabetes

William B. White, M.D., Christopher P. Cannon, M.D., Simon R. Heller, M.D., Steven E. Nissen, M.D., Richard M. Bergenstal, M.D., George L. Bakris, M.D., Alfonso T. Perez, M.D., Penny R. Fleck, M.B.A., Cyrus R. Mehta, Ph.D., Stuart Kupfer, M.D., Craig Wilson, Ph.D., William C. Cushman, M.D., and Faiez Zannad, M.D., Ph.D., for the EXAMINE Investigators*

End Point	Placebo (N=2679)	Alogliptin (N=2701)	Hazard Ratio for Alogliptin Group (95% CI)	P Value*
	no. (%)			
Primary end point†	316 (11.8)	305 (11.3)	0.96 (≤1.16)‡	0.32
Components of primary end point				
Death from cardiovascular causes	111 (4.1)	89 (3.3)	0.79 (0.60–1.04)	0.10
Nonfatal myocardial infarction	173 (6.5)	187 (6.9)	1.08 (0.88–1.33)	0.47
Nonfatal stroke	32 (1.2)	29 (1.1)	0.91 (0.55–1.50)	0.71
Principal secondary end point§	359 (13.4)	344 (12.7)	0.95 (≤1.14)‡	0.26
Other end points				
Death from any cause	173 (6.5)	153 (5.7)	0.88 (0.71–1.09)	0.23
Death from cardiovascular causes¶	130 (4.9)	112 (4.1)	0.85 (0.66–1.10)	0.21

EXAMINE e ICC

- Análisis post hoc eliminando el punto final de muerte del punto primario
- HR de falla cardíaca 1.19 (p 0.22)
- Consideraciones:
  - Cambiaron la definición de falla cardíaca
  - Análisis post hoc
- Cuando se combinan los datos de SAVOR y EXAMINE HR 1.24 (IC 1.07-1.45)

EASD Barcelona 2013

VIVIDD

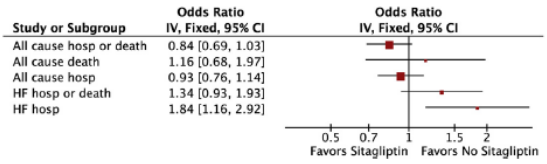
- Vildagliptin in ventricular dysfunction diabetes trial
- Estudio de no inferioridad en 254 pacientes con ICC, NYHA I-III
- Aumento en volumen ventricular izquierdo telediastólico y volumen telesistólico

Sitagliptina e ICC

Outcome	Agent	Exposed Cases/Total Exposed	Unexposed Cases/Total Unexposed	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)	p Value*
All-cause death or hospital admission	Sitagliptin	113/1,588	4,024/43,846	0.75 (0.62-0.92)	0.84 (0.69-1.03)	0.10
	Metformin	756/10,734	3,381/34,700	0.64 (0.59-0.70)	0.78 (0.71-0.85)	<0.001
	Insulin	800/7,149	3,337/38,285	1.37 (1.25-1.50)	1.16 (1.05-1.28)	0.004
	Sulfonylurea	673/7,710	3,464/37,724	0.94 (0.86-1.03)	1.10 (1.00-1.23)	0.043
	Other	109/1,429	4,028/44,005	0.81 (0.67-1.00)	0.95 (0.77-1.17)	0.64
All-cause death	Sitagliptin	19/274	389/4,193	0.73 (0.45-1.18)	1.16 (0.68-1.97)	0.59
	Metformin	66/1,530	342/2,937	0.33 (0.25-0.44)	0.52 (0.37-0.71)	<0.001
	Insulin	142/1,411	266/3,056	1.18 (0.95-1.47)	1.11 (0.84-1.47)	0.46
	Sulfonylurea	73/1,247	335/3,220	0.53 (0.41-0.69)	0.83 (0.61-1.14)	0.25
	Other	13/214	395/4,253	0.63 (0.36-1.12)	0.87 (0.46-1.63)	0.66
All-cause hospital admission	Sitagliptin	112/1,489	3,964/43,274	0.80 (0.6-0.98)	0.93 (0.76-1.14)	0.46
	Metformin	750/10,556	3,326/34,207	0.65 (0.59-0.71)	0.79 (0.71-0.87)	<0.001
	Insulin	795/7,215	3,281/37,548	1.34 (1.23-1.47)	1.13 (1.03-1.25)	0.014
	Sulfonylurea	669/7,683	3,407/37,080	0.93 (0.85-1.03)	1.08 (0.97-1.19)	0.15
	Other	109/1,277	3,967/43,486	0.93 (0.76-1.13)	1.06 (0.86-1.31)	0.56
HF-related hospital admission or death	Sitagliptin	37/409	1,109/12,172	0.99 (0.70-1.41)	1.34 (0.93-1.92)	0.12
	Metformin	154/2,556	992/10,025	0.53 (0.44-0.64)	0.70 (0.57-0.86)	0.001
	Insulin	217/2,126	929/10,455	1.20 (1.01-1.42)	1.02 (0.84-1.24)	0.81
	Sulfonylurea	156/2,063	990/10,518	0.76 (0.63-0.92)	0.92 (0.75-1.13)	0.41
	Other	21/302	1,125/12,279	0.74 (0.47-1.16)	0.85 (0.53-1.36)	0.50
HF-related hospital admission	Sitagliptin	25/200	799/8,862	1.47 (0.95-2.27)	1.84 (1.16-2.92)	0.01
	Metformin	106/1,378	718/7,684	0.76 (0.60-0.96)	0.87 (0.66-1.12)	0.28
	Insulin	113/1,114	711/7,948	1.19 (0.94-1.50)	0.97 (0.75-1.27)	0.83
	Sulfonylurea	103/1,067	721/7,995	1.09 (0.86-1.39)	1.11 (0.84-1.45)	0.47
	Other	14/147	810/8,905	0.98 (0.56-1.72)	1.08 (0.59-1.96)	0.81

Weir D. JACC: Heart Failure. 2014

Sitagliptina e ICC



Weir D. JACC: Heart Failure. 2014

Análisis

- Con estos datos e ICC
  - Saxagliptina: SAVOR
  - Alogliptina: EXAMINE
  - Vildagliptina: VIVIDD
  - Sitagliptina: estudio de Weir et al
- Será un efecto de clase?
- A la espera de TECOS y CAROLINA
- Conducta actual

SEGURIDAD PANCREÁTICA

Pancreatitis

- SAVOR y EXAMINE evaluaron de forma prospectiva y de manera predefinida la incidencia de pancreatitis. No diferencias significativas.
- EMA y FDA se pronunciaron en cuanto a seguridad en riesgo de pancreatitis
- No hay datos suficientes para afirmar que hay aumento en riesgo de cáncer de páncreas

Conclusiones

- Los inhibidores de DPP-4 en general son una clase donde es difícil diferenciar entre los agentes
- Saxagliptin/metformin XR es la única formulación combinada que permite administrarlo una vez al día
- Falta de adherencia se asocia a mayor morbilidad
- Precaución en pacientes con historia de falla cardíaca, insuficiencia renal o proteinuria

Preguntas…
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