I JORNADA d'Actualització en Risc Cardiovascular

de la VOCALIA DE TARRAGONA de la CAMFiC

14 de novembre de 2013
Hotel Ciutat de Tarragona

Jesús Vizcaíno: Novetats en el maneig farmacològic de la diabetis.

camfic
societat catalana de medicina familiar i comunitària

Inside Guidelines

Comparative analysis of recommendations and evidence in diabetes guidelines from 13 countries

Diabetes Care 25:1933–1939, 2002

Country (ID code)	Organization responsible for guideline development	Title in English	Year of publication
Australia (AU)	NSW (New South Wales) Health Department	Improving diabetes care and outcomes. Principles of care and guidelines for the clinical management of diabetes mellitus	1996
Canada (CA)	Canadian Medical Association	Clinical practice guidelines for the management of diabetes in Canada	1998
Denmark (DK)	Danish College of General Practitioners	Non insulin demanding diabetes - NIDDM. A practical guidance for therapists	1998
England (EN)	East London Clinical Guidelines Project. Department of General Practice and Primary Care	Clinical guidelines for the management of diabetes in East London	1996
Finland (FI)	Finnish Diabetes League	Type II diabetes clinical guideline	1994
France (FR)	Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES)	a. Strategy for monitoring of type 2 diabetics, excluding monitoring of complications	1999
		b. Strategy for management of type 2 diabetics, excluding management of complications	2000
Italy (IT)	Italian Society for Diabetology	Diabetes mellitus. Practical guide for diagnosis and treatment	1997
The Netherlands (NL1)	Dutch Institute for Healthcare Improvement CBO	Guidelines diabetic nephropathy and cardiovascular diseases with diabetes mellitus	1998
The Netherlands (NL2)	Dutch College of General Practitioners (NHG)	Practice guideline diabetes mellitus	1999
New Zealand (NZ)	New Zealand Guidelines Group	Guidelines for the management of core aspects of diabetes care	1999
Scotland (SC)	Scottish Intercollegiate Guidelines	Management of diabetic cardiovascular disease	1997
Spain (SP)	Catalan Society of Primary Care	Guideline on treatment of diabetes mellitus type 2 in primary care	1996
Switzerland (SW)	University Hospital of Geneva	Detection of diabetes mellitus. Guidelines for the outpatient's clinic	1996
USA (US1)	American Diabetes Association	Standards of medical care for patients with diabetes mellitus	2000
USA (US2)	Institute for Clinical System Improvements	Management of type 2 diabetes mellitus	2000

Inside Guidelines

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Diabetes Care 25:1933–1939, 2002

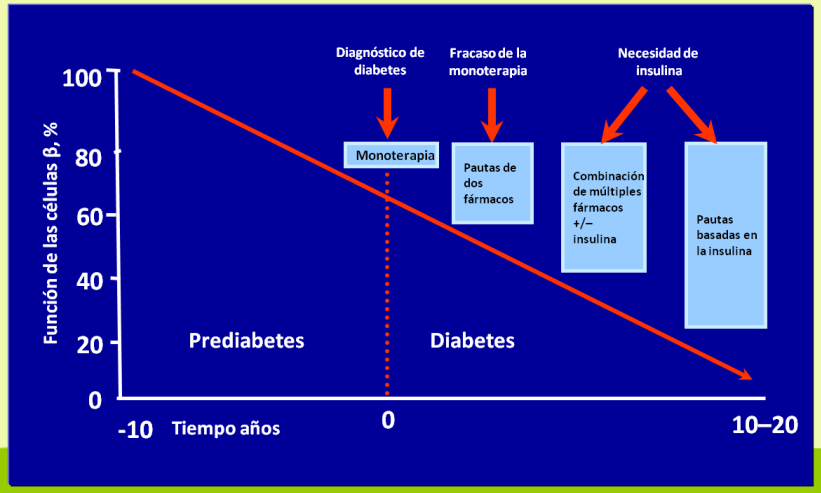
5) poor glycemic control should be tackled initially with diet alone, followed by oral medication and insulin if necessary, unless the patient is acutely unwell;

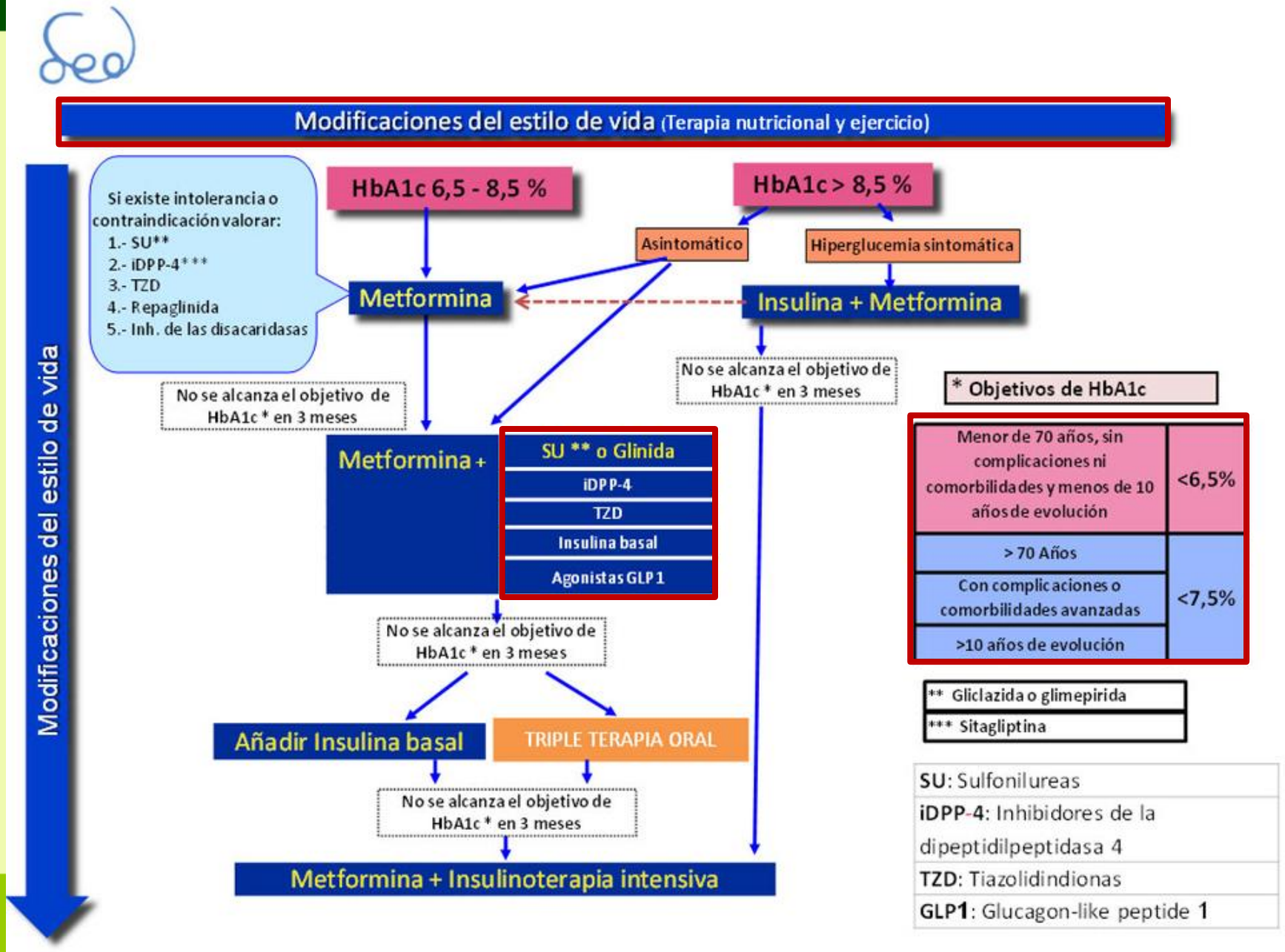
6) ***sulfonylureas or biguanides*** are recommended in patients with normal BMI, and ***metformin*** is recommended in obese patients;

7) a second oral agent should be added to maximum doses of an initial agent in case of poor glygemic control;

8) **HbA1c** is suitable for long-term monitoring and should be **8%**;

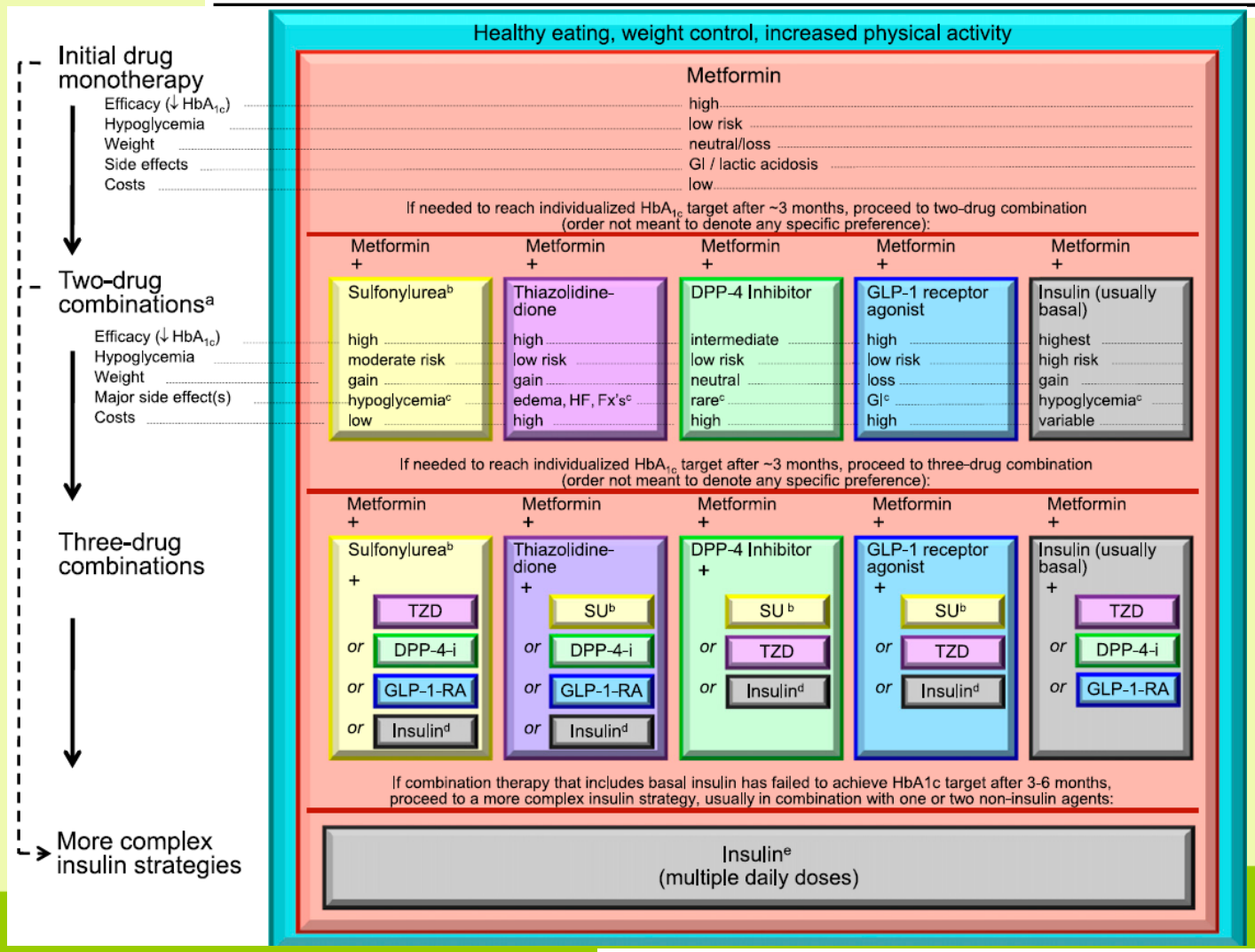
9) if on **insulin**, self-monitoring of blood glucose is recommended;




Modificaciones del estilo de vida (Terapia nutricional y ejercicio)
Modificaciones del estilo de vida
Si existe intolerancia o contraindicación valorar:
1.- SU**
2.- iDPP-4***
3.- TZD
4.- Repaglinida
5.- Inh. de las disacaridasas
HbA1c 6,5 - 8,5 %
HbA1c > 8,5 %
Asintomático
Hiperglucemia sintomática
Metformina
Insulina + Metformina
No se alcanza el objetivo de HbA1c * en 3 meses
No se alcanza el objetivo de HbA1c * en 3 meses
Metformina +
SU ** o Glinida
iDPP-4
TZD
Insulina basal
Agonistas GLP1
No se alcanza el objetivo de HbA1c * en 3 meses
Añadir Insulina basal
TRIPLE TERAPIA ORAL
No se alcanza el objetivo de HbA1c * en 3 meses
Metformina + Insulinoterapia intensiva
* Objetivos de HbA1c
Menor de 70 años, sin complicaciones ni comorbilidades y menos de 10 años de evolución
<6,5%
> 70 Años
Con complicaciones o comorbilidades avanzadas
>10 años de evolución
<7,5%
** Gliclazida o glimepirida
*** Sitagliptina
SU: Sulfonilureas
iDPP-4: Inhibidores de la dipeptidilpeptidasa 4
TZD: Tiazolidindionas
GLP1: Glucagon-like peptide 1

Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach

Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)



Diabetes Care Publish Ahead of Print, published online April 19, 2012

Glycemic Control Algorithm

LIFESTYLE MODIFICATION
(Including Medically Assisted Weight Loss)

ENTRY A1c < 7.5%

MONOTHERAPY*

- Metformin
- GLP-1 RA
- DPP4-i
- AG-i
- SGLT-2 **
- TZD
- SU/GLN

If A1c > 6.5% in 3 months add second drug (Dual Therapy)

ENTRY A1c ≥ 7.5%

DUAL THERAPY*

MET or other first-line agent +

- GLP-1 RA
- DPP4-i
- TZD
- ** SGLT-2
- Basal insulin
- Colesevelam
- Bromocriptine QR
- AG-i
- SU/GLN

If not at goal in 3 months proceed to triple therapy

TRIPLE THERAPY*

MET or other first-line agent + 2ND LINE AGENT

- GLP-1 RA
- TZD
- ** SGLT-2
- Basal insulin
- DPP4-i
- Colesevelam
- Bromocriptine QR
- AG-i
- SU/GLN

If not at goal in 3 months proceed to or intensify insulin therapy

ENTRY A1c > 9.0%

NO SYMPTOMS	SYMPTOMS
DUAL THERAPY OR TRIPLE THERAPY	INSULIN ± OTHER AGENTS

ADD OR INTENSIFY INSULIN

* Order of medications listed are a suggested hierarchy of usage

** Based upon phase 3 clinical trials data

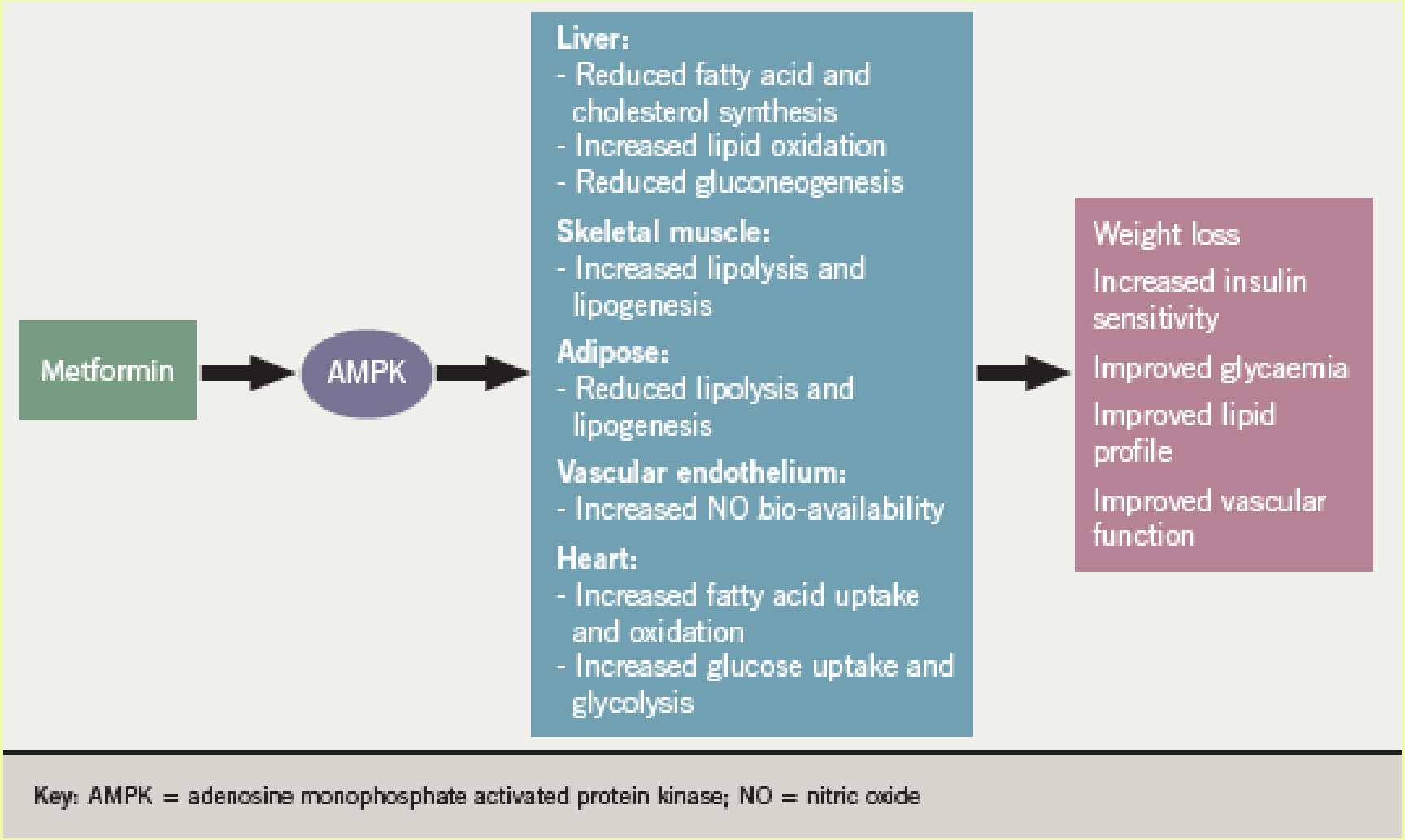
LEGEND

✓ = Few adverse events or possible benefits

⚠ = Use with caution

PROGRESSION OF DISEASE

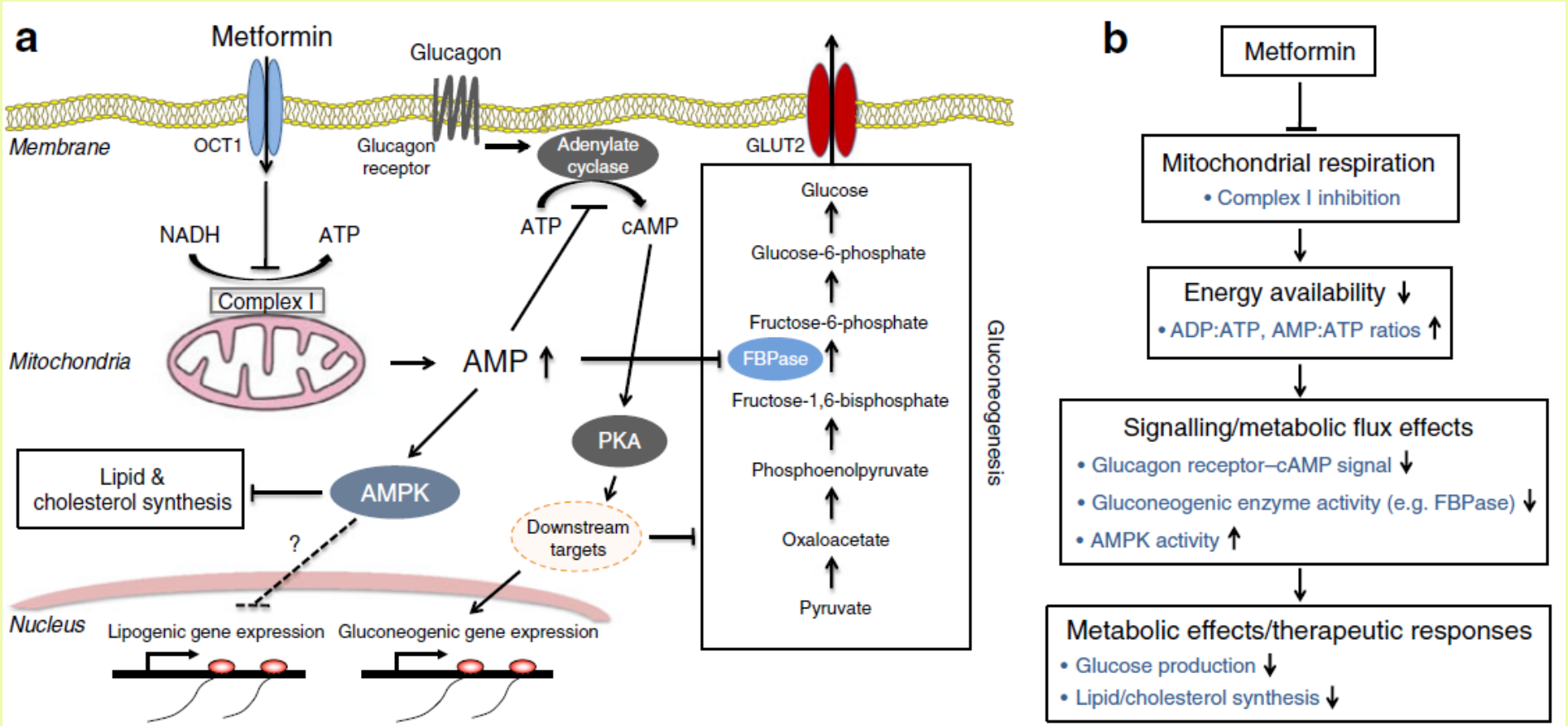
METFORMINA



Boyle J.G, McKay G.A, Fisher M. Drugs for diabetes: part 1 metformin. Br J Cardiol 2010;17:231.

Molecular mechanism of action of metformin: old or new insights?

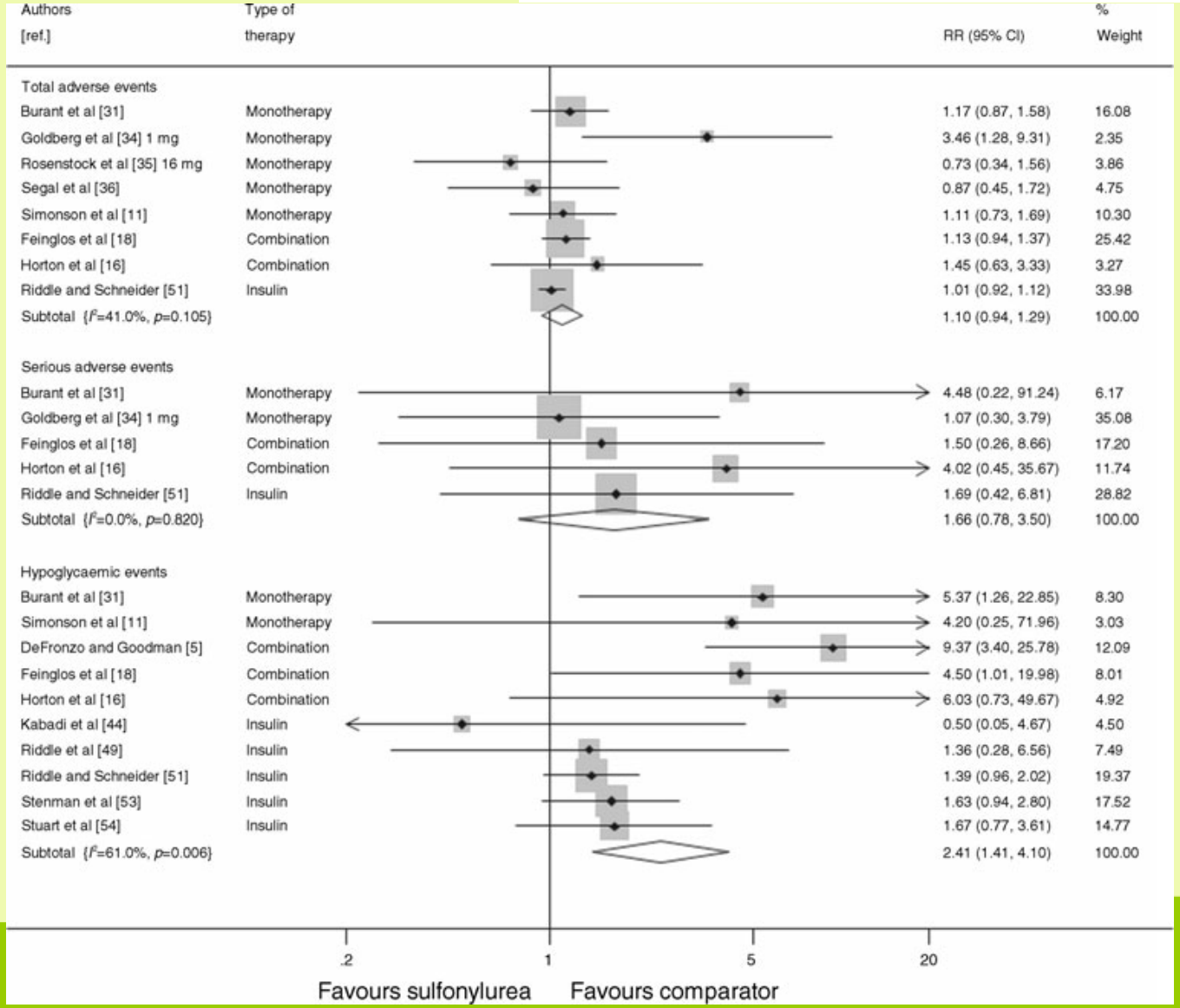
Graham Rena · Ewan R. Pearson · Kei Sakamoto



Diabetologia (2013) 56:1898–1906

Estimating the effect of sulfonylurea on HbA_{1c} in diabetes: a systematic review and meta-analysis

J. A. Hirst · A. J. Farmer · A. Dyar · T. W. C. Lung · R. J. Stevens

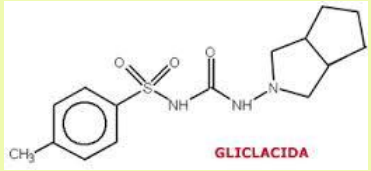


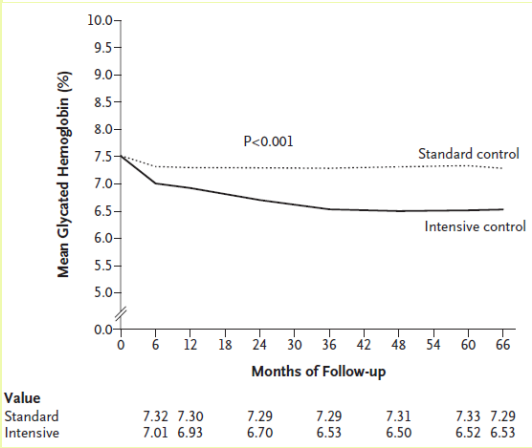
Diabetologia (2013) 56:973–984

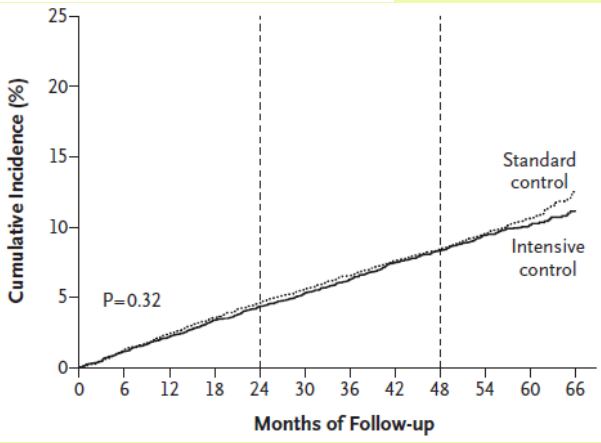
La **Organización Mundial de la Salud (OMS)** ha catalogado la **gliclazida**, como medicamento esencial en el tratamiento de diabetes tipo 2 al ser incluido en la nueva **Lista de Medicamentos Esenciales**

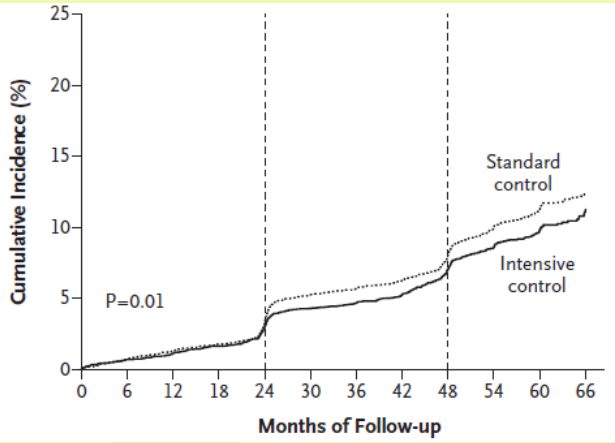

Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes

The ADVANCE Collaborative Group*









TIAZOLINDINDIONAS

Safety Announcement
[15-6-2011] The **U.S. Food and Drug Administration (FDA)** is informing the public that use of the diabetes medication **Actos (pioglitazone)** for more than one year **may be associated with an increased risk of bladder cancer**. Information about this risk will be added to the *Warnings and Precautions* section of the label for pioglitazone-containing medicines. The patient Medication Guide for these medicines will also be revised to include information on the risk of bladder cancer.

FDA Drug Safety Communication: Ongoing Safety Review of Actos (pioglitazone) and Potential Increased Risk of Bladder Cancer After Two Years Exposure

17-09-2010 Bladder cancer is estimated to occur in 20 per 100,000 persons per year in the United States and is thought to be higher in diabetics.

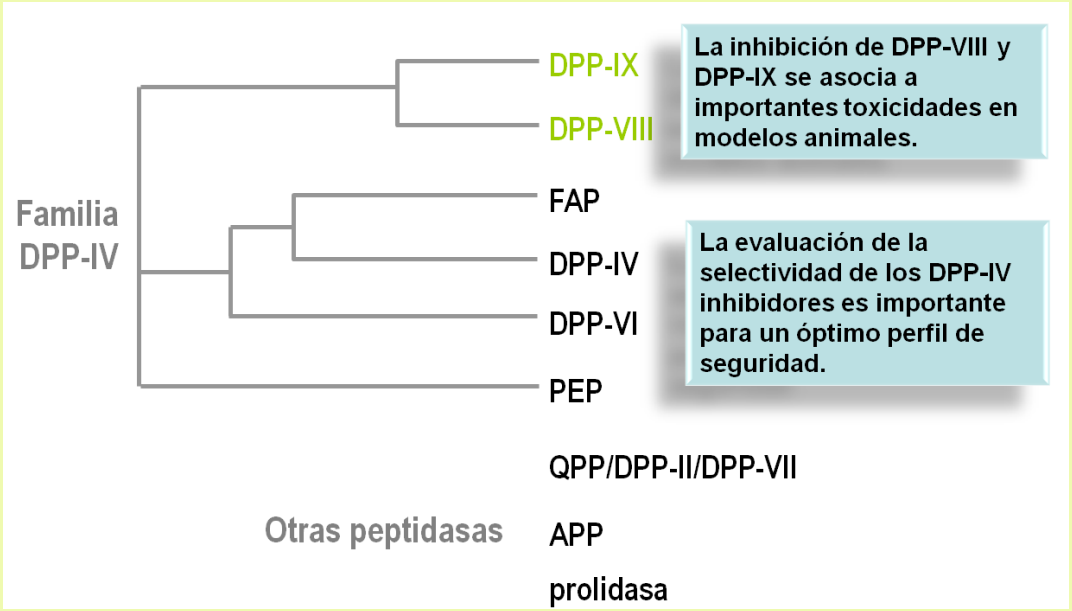
TIAZOLINDINDIONAS

Safety Announcement

[18-5-2011] The **U.S. Food and Drug Administration (FDA**) is informing the public of new **restrictions to the prescribing and use of rosiglitazone**-containing medicines. These medicines to treat type II diabetes are sold under the names Avandia, Avandamet, and Avandaryl. Healthcare providers and patients must enroll in a special program in order to prescribe and receive these drugs.

The new restrictions are part of a Risk Evaluation and Mitigation Strategy (REMS)—a program FDA may require to manage serious risks of marketed drugs. The restrictions are based on data that suggested an **elevated risk of heart attacks** in patients treated with **rosiglitazone**. The decision to restrict access to rosiglitazone medicines was made on September 23, 2010.

ESPECIFICIDAD



DPP-IV: dipeptidil peptidasa-IV;
FAP: proteína activadora de los fibroblastos;
PEP: prolil endopeptidasa;
QPP: *quiescent cell proline dipeptidase*.;
APP: aminopeptidasa P.

Lankas GR, et al. *Diabetes*. 2005; 54: 2988-2994.

Fármaco	Selectividad	QPP /DPP-II	PEP	FAP α	DPP-VIII	DPP-IX
Sitagliptina	Alta	> 5.550	> 5.550	> 5.550	> 2.660	> 5.550
Vildagliptina	Moderada	> 100.000	60.000	285	270	32
Saxagliptina	Moderada	> 50.000	No comunicado	> 4.000	390	77
Linagliptina	Moderada	> 100.000	> 100.000	89	40.000	> 10.000

Matsuyama-Yokono A, et al. Biochem Pharmacol. 2008; 76(1): 98-107

INDICACIONES Y ASOCIACIONES

	Sitagliptina	Vildagliptina	Saxagliptina	Linagliptina
Modo de administración:	**1 al día**	**2 al día** **1 x día** (con SU reducción de dosis)	**1 al día**	**1 al día**
Monoterapia	*	*	✗	**
Asociado a metformina	✓	✓	✓	✓
Asociado a sulfonilurea	✓	✓	✓	✗
Asociado a glitazonas	✓	✓	✓	✗
Triple terapia con merformina + sulfonilurea	✓	✗	✗	✓
Triple terapia con merformina + glitazonas	✓	✗	✗	✗
Añadido a insulina	✓	✗	✓	✗

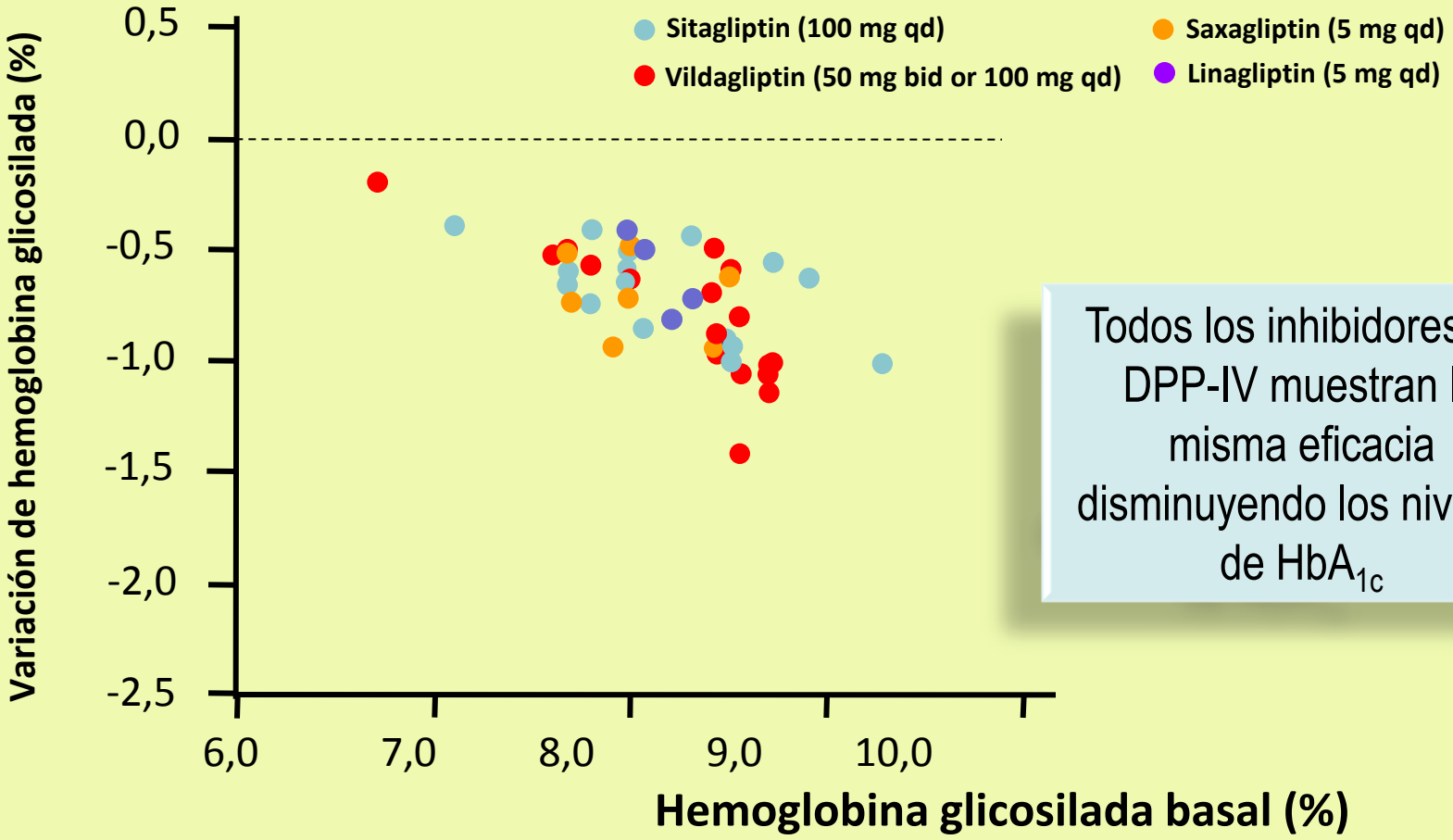
* **En caso de contraindicación o intolerancia a metformina**

** **En pacientes controlados inadecuadamente con dieta y ejercicio por sí solos y en los que la metformina no es adecuada por intolerancia o está contraindicada debido a I. Renal**

EMEA: Agencia Europea de Medicinas. AGEMED: Agencia Española del Medicamento y Productos Sanitarios

EFICACIA IDPP-IV

Estudios de ≥ 12 semanas de duración



Todos los inhibidores de DPP-IV muestran la misma eficacia disminuyendo los niveles de HbA_{1c}

Adaptado de: Deacon C. *Diab Obes Metab.* 2011; 13: 7-18

POBLACIONES ESPECIALES

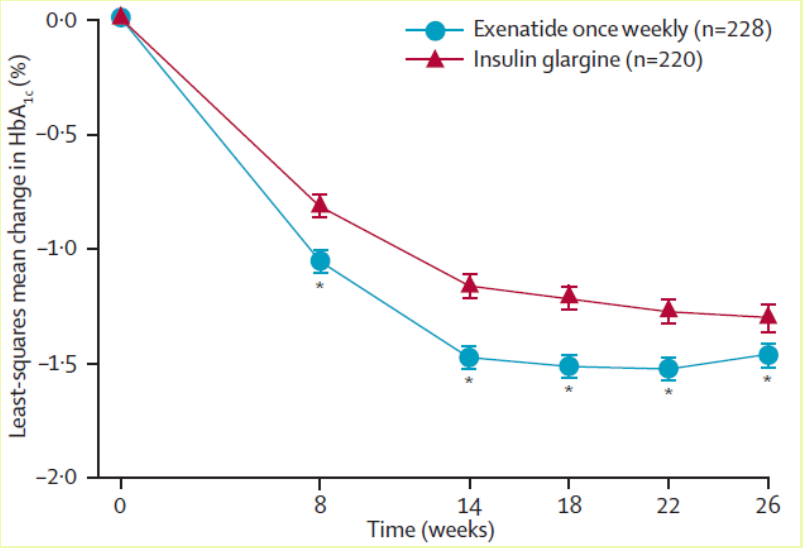
	I. Renal			I. Hepática	
	Leve (Acl Cr ≥ 50 ml/min)	**Moderada** (Acl Cr ≥ 30- < 50 mg/ml)	**Grave/terminal** (Acl Cr < 30 ml/min)	**Leve/moderada** Child-Pugh 5-9	**Grave** Child-Pugh ≥ 10
Sitagliptina	√	½ dosis 50mg	¼dosis 25mg	√	No se dispone de experiencia clínica
Vildagliptina	√	½ dosis	½ dosis	No recomendado	No recomendado
Saxagliptina	√	½ dosis	½ dosis/No recomendado*	Leve: √ Moderada: Precaución	No recomendado
Linagliptina	√	√	√	√	No se dispone de experiencia clínica
Alogliptina	√	½ dosis	½ dosis	√	No se dispone de experiencia clínica

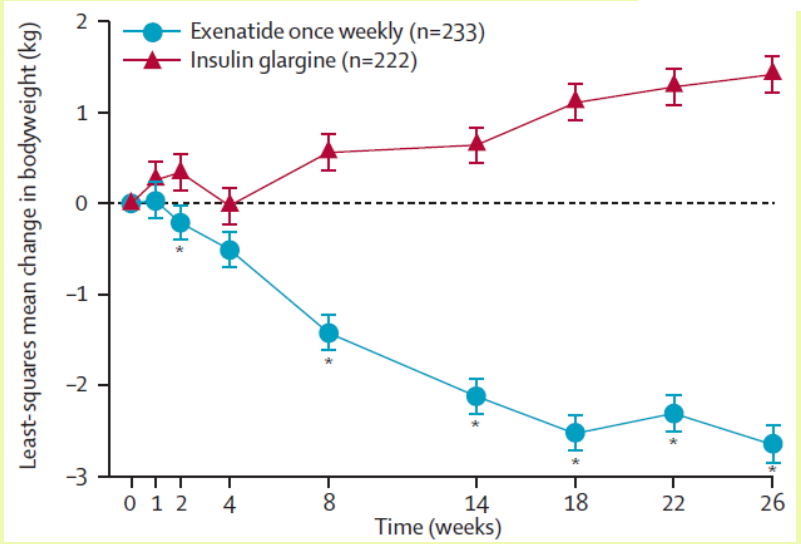
***No recomendado si enfermedad renal terminal con diálisis.**
Vildagliptina precisa monitorización hepática .

Once weekly exenatide compared with insulin glargine titrated to target in patients with type 2 diabetes (DURATION-3): an open-label randomised trial

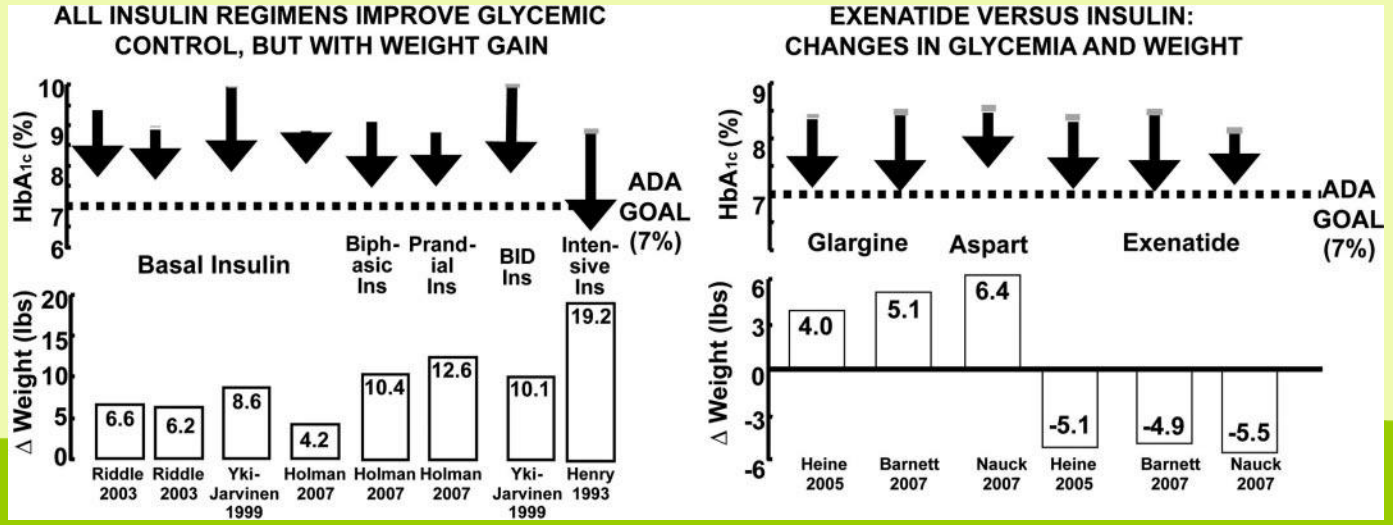
Michaela Diamant, Luc Van Gaal, Stephen Stranks, Justin Northrup, Dachuang Cao, Kristin Taylor, Michael Trautmann

Lancet 2010; 375: 2234–43





Effect of insulin (Ins) and exenatide on A1C and body weight in type 2 diabetic subjects



Once weekly exenatide compared with insulin glargine titrated to target in patients with type 2 diabetes (DURATION-3): an open-label randomised trial

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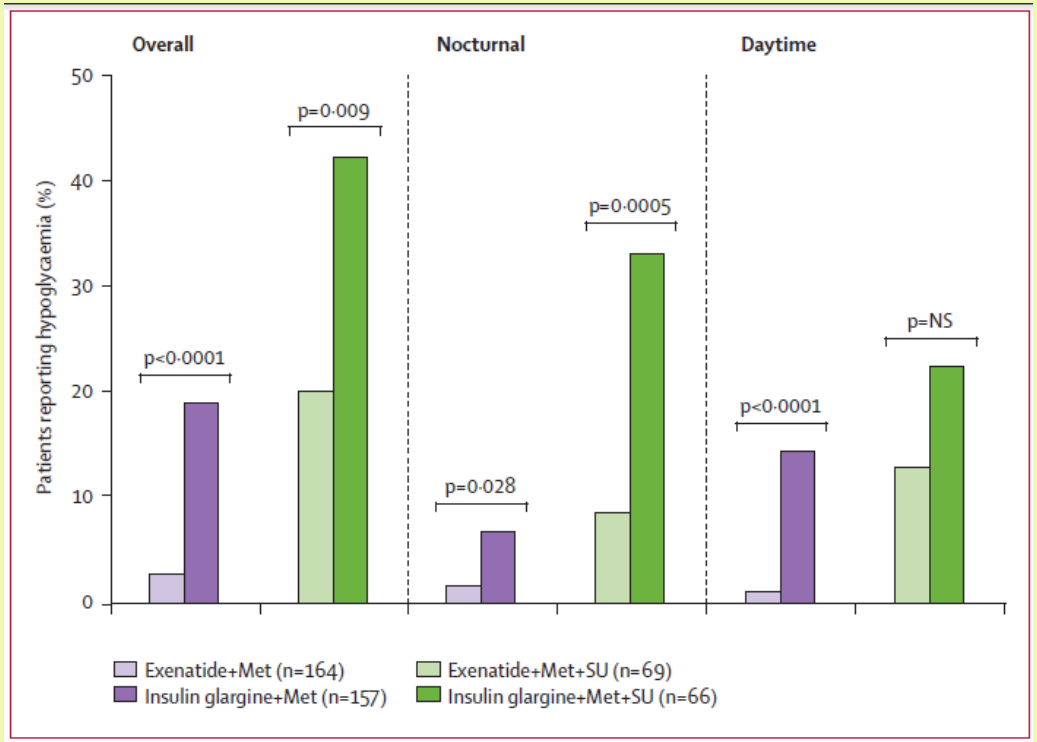
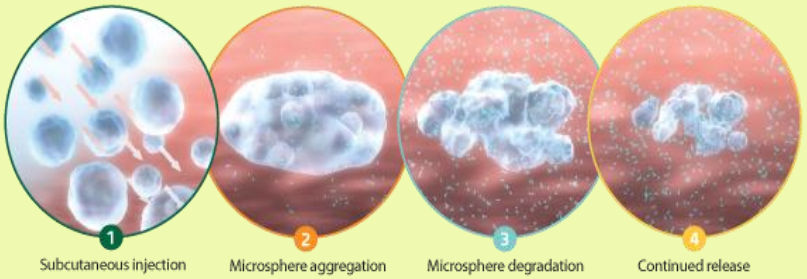
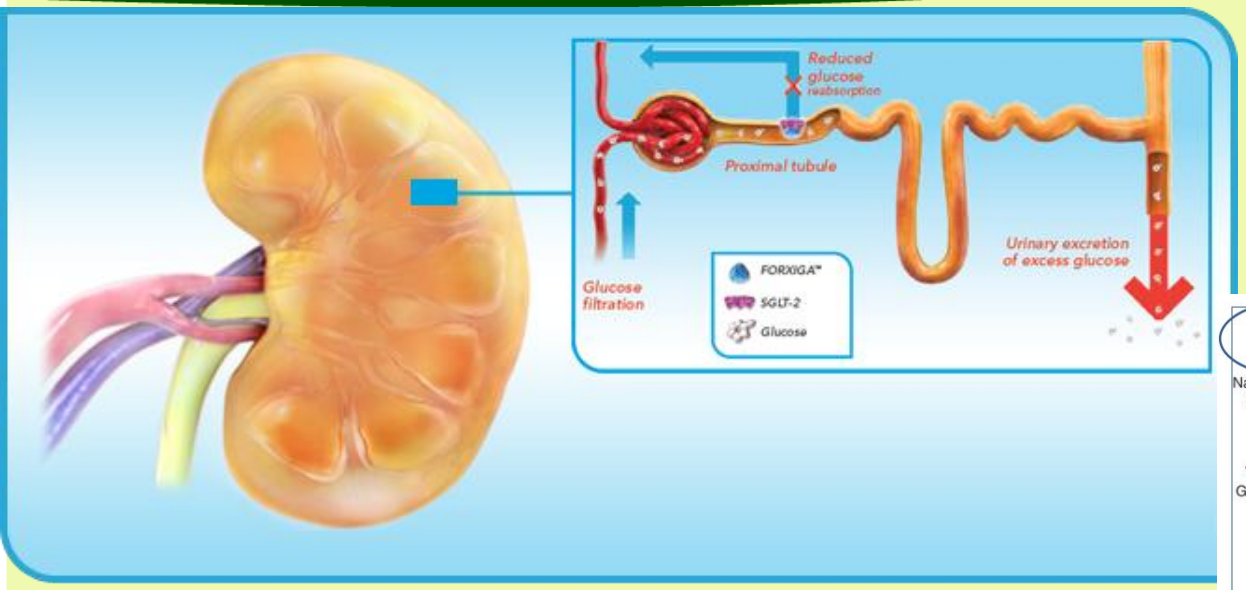


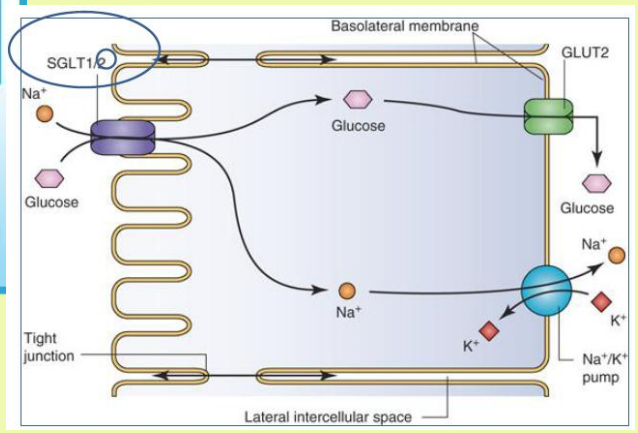
Figure 6: Rates of confirmed minor hypoglycaemia in patients taking exenatide once weekly or insulin glargine titrated to target, by oral blood-glucose-lowering treatment
Met=metformin. SU=sulphonylurea. NS=not significant.



Close-up of a microsphere dissolving, continuously releasing medicine over time.

INHIBIDORES SGLT2





	SGLT1	SGLT2
Site	Intestine, kidney	Kidney
Renal location	Late proximal straight tubule (S3 segment)	Early proximal convoluted tubule (S1 segment)
Sugar specificity	Glucose or galactose	Glucose
Glucose affinity	High (K_m=0.4 mM)	Low (K_m=2 mM)
Glucose transport capacity	Low	High
Renal glucose reabsorption (%)	~10%	~90%
Role	Dietary absorption of glucose and galactose, renal glucose reabsorption. Mutation in the gene for SGLT1 results in carbohydrate malabsorption and severe diarrhea	Renal glucose reabsorption. Inhibition of SGLT2 as a rational target of therapy for T2DM is based on pathology of familial renal glycosuria

SGLT: Sodium–glucose co-transporter, T2DM: Type 2 diabetes mellitus, Data from Ref.[5,10]

Inhibitors of type 2 sodium glucose co-transporters – a new strategy for diabetes treatment

Pharmacol Rep. 2009 Sep-Oct;61(5):778-84.

Aleksandra Bołdys, Bogusław Okopień

SGLT2 inhibitor	Clinical development	Clinical study	Dose of medication (mg)	Blood glucose reduction (mg%)
Dapagliflozin	III phase	12-weeks prospective, randomized parallel-group, double-blind, placebo- controlled (study from the II phase)	2.5, 5, 10, 20, 50	16–31
Remogliflozin	II phase	randomized, double-blind, parallel assignment, safety/efficacy study	no publication to date	no publication to date
Sergliflozin	II phase	double-blind, randomized, placebo-controlled study (evaluation weight loss, safety, tolerability and pharmacokinetics in obese subjects following 12-week dosing*	500, 1000 *	–
AVE - 2268	phase IIb	–	–	–
JNJ-28431754	II phase	double-blind, randomized, placebo-controlled, double-dummy, parallel group, multicenter, dose-ranging	50, 100, 200, 300	no publication up to date
ISIS 388626	Preclinical	–	–	–

Sodium Glucose Co-transporter Type 2 (SGLT2) Inhibitors: Targeting the Kidney to Improve Glycemic Control in Diabetes Mellitus

Diabetes Therapy 2013 Oct 19.

Table 2 SGLT2 inhibitors in clinical development

Compound	Sponsor	Development phase	Expected approval/launch date
Dapagliflozin	Bristol Myers Squibb, AstraZeneca	3	EMA approval given in November 2012; recent NDA resubmission to FDA
Canagliflozin	Janssen (Johnson & Johnson), Mitsubishi Tanabe	3	FDA approval given in March 2013; EMA decision awaited
Empagliflozin	Boehringer Ingelheim, Lilly	3	Applications filed with FDA (NDA) and with EMA (MAA) in March 2013
Ipragliflozin	Astellas, Kotobuki	3	Marketing approval filed with Japanese regulatory body in March 2013
Luseogliflozin	Taisho	3	Marketing approval filed with Japanese regulatory body in April 2013
Tofogliflozin	Chugai, Kowa, Sanofi	3	Marketing approval filed with Japanese regulatory body in June 2013
Ertugliflozin (PF04971729)	Pfizer, Merck & Co.	2	Not applicable
LX4211	Lexicon Pharmaceuticals	2	Not applicable
EGT0001442	Theracos	2	Not applicable

EMA European Medicines Agency, *FDA* Food and Drug Administration (United States), *MAA* marketing authorization application, *NDA* New Drug Application, *SGLT2* sodium glucose co-transporter

GLITAZARES

Am Heart J. 2013 Sep;166(3):429-34. doi: 10.1016/j.ahj.2013.05.013. Epub 2013 Jul 26.

Evaluation of the dual peroxisome proliferator-activated receptor α/γ agonist aleglitazar to reduce cardiovascular events in patients with acute coronary syndrome and type 2 diabetes mellitus: rationale and design of the AleCardio trial.

Lincoff AM, Tardif JC, Neal B, Nicholls SJ, Rydén L, Schwartz GG, Malmberg K, Buse JB, Henry RR, Wedel H, Weichert A, Cannata R, Grobbee DE.

The safety concerns relate to 3 things: bone fractures, heart failure, and gastrointestinal bleeding

Conclusions: AleCardio will establish whether the PPAR-α/γ agonist aleglitazar improves cardiovascular outcomes in patients with diabetes and high-risk coronary disease.

Retirada de los otros glitazares en estudio en el 2006:

- **Muraglitazar (aumento del riesgo cardiovascular)**
- **Tesaglitazar (problemas renales)**

Lancet. 2012 Apr 21;379(9825):1498-507. doi: 10.1016/S0140-6736(12)60205-0.

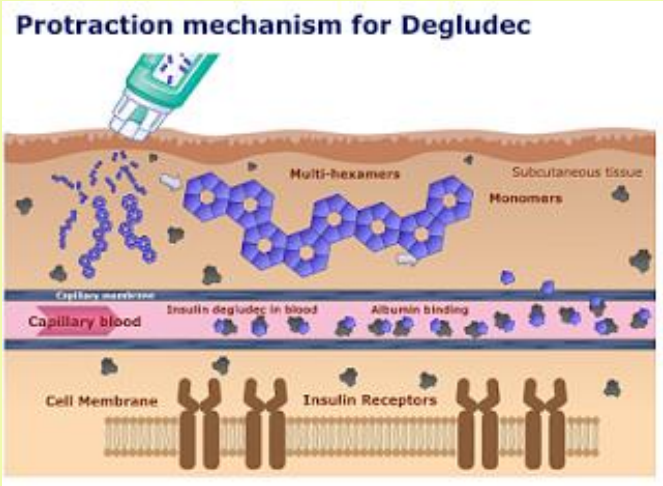
Insulin degludec, an ultra-longacting basal insulin, versus insulin glargine in basal-bolus treatment with mealtime insulin aspart in type 2 diabetes (BEGIN Basal-Bolus Type 2): a phase 3, randomised, open-label, treat-to-target non-inferiority trial.

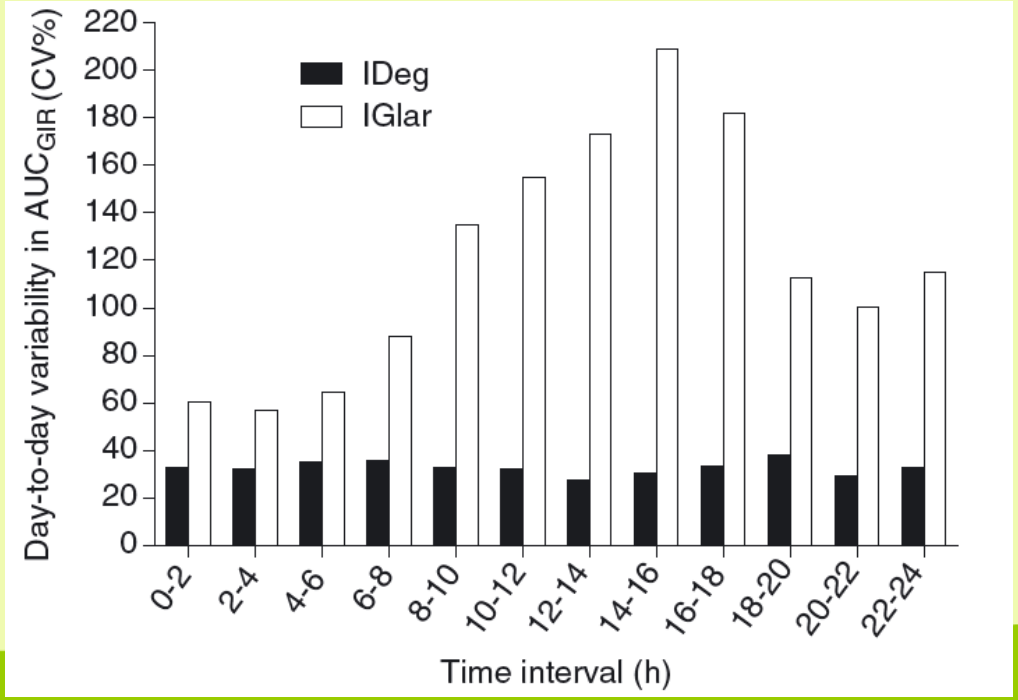
Garber AJ, King AB, Del Prato S, Sreenan S, Balci MK, Muñoz-Torres M, Rosenstock J, Endahl LA, Francisco AM, Hollander P; NN1250-3582 (BEGIN BB T2D) Trial Investigators.

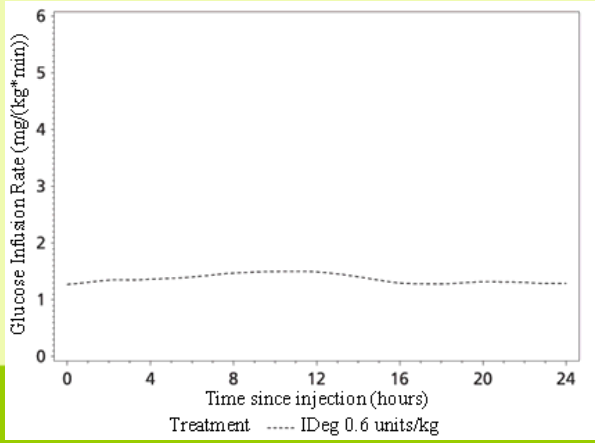
Tresiba® and Ryzodeg® receive marketing authorisations in Europe (21 January 2013)

Read the full announcement in PDF format

Bagsværd, Denmark, 21 January 2013 - Novo Nordisk today announced that the European Commission has granted marketing authorisations for Tresiba® (insulin degludec) and Ryzodeg® (insulin degludec/insulin aspart) for the treatment of diabetes in adults. The authorisations cover all 27 European Union member states.

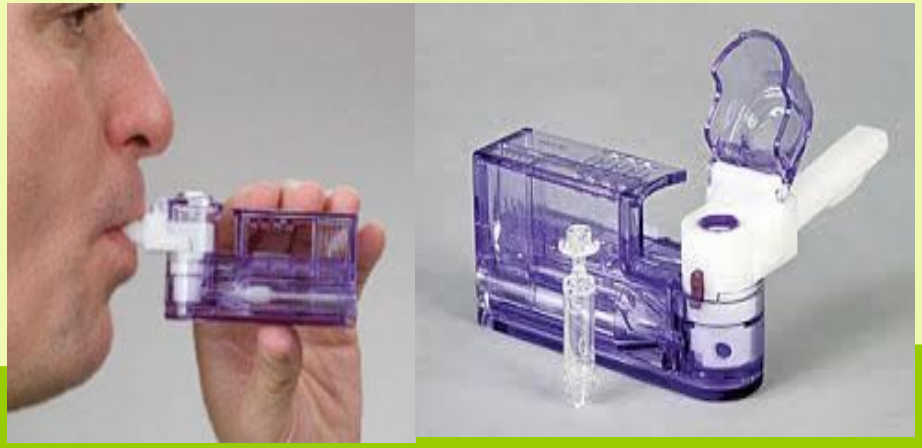






INSULINAS ALTERNATIVAS

- Nasal
- Bucal
- Oral
- Inhalada
- Transdérmica



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Insulin	Sensitizers	Biguanides		Metformin[#] · Buformin[‡] · Phenformin[‡]
		TZDs/"glitazones" (PPAR)		Pioglitazone · Rivoglitazone[†] · Rosiglitazone · Troglitazone[‡]
		Dual PPAR agonists		Aleglitazar[†] · Muraglitazar[§] · Saroglitazar · Tesaglitazar[§]
	Secretagogues	K+ ATP	Sulfonylureas	*1st generation*: Acetohexamide · Carbutamide · Chlorpropamide · Metahexamide · Tolbutamide · Tolazamide *2nd generation*: Glibenclamide (Glyburide)[#] Glibornuride · Glipizide · Gliquidone · Glisoxepide · Glyclopyramide · Glimepiride · Gliclazide
			Meglitinides/"glinides"	Nateglinide · Repaglinide · Mitiglinide
		GLP-1 agonists		Exenatide · Liraglutide · Taspoglutide[†] · Albiglutide[†] · Lixisenatide
		DPP-4 inhibitors		Alogliptin · Anagliptin · Gemigliptin · Linagliptin · Saxagliptin · Sitagliptin · Teneligliptin · Vildagliptin
		GPR40 Free fatty acid receptor 1		Fasiglifam[†]
	Analogs/other insulins			*fast-acting* (Insulin lispro · Insulin aspart · Insulin glulisine) · *short-acting* (Regular insulin) · *long-acting* (Insulin glargine · Insulin detemir · NPH insulin *ultra-long-acting* (**Insulin degludec**[†]) · *inhalable* Exubera[‡]
Other	Alpha-glucosidase inhibitors			Acarbose · Miglitol · Voglibose
	Amylin analog			Pramlintide
	SGLT2 inhibitors			Canagliflozin · Dapagliflozin · Empagliflozin[†] · Remogliflozin[§] · Sergliflozin[§] · Tofogliflozin[†]
	Other			Bromocriptine · Benfluorex[‡] · Tolrestat[‡]

[#]WHO-EM · [‡]Withdrawn from market · Clinical trials: ([†]Phase III · [§]Never to phase III)

Profiles of Antidiabetic Medications

	MET	DPP-4i	GLP-1 RA	TZD	AGI	COLSVL	BCR-QR	SU / GLN	INSULIN	SGLT-2	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/Severe / Mild	Moderate to Severe	Neutral	Neutral
WEIGHT	Slight Loss	Neutral	Loss	Gain	Neutral	Neutral	Neutral	Gain	Gain	Loss	Loss
RENAL/ GU	Contra-indicated Stage 3B,4,5	Dose Adjustment May be Necessary (Except Linagliptin)	Exenatide Contra-indicated CrCl < 30	May Worsen Fluid Retention	Neutral	Neutral	Neutral	More Hypo Risk	More Hypo Risk & Fluid Retention	Infections	Neutral
GI Sx	Moderate	Neutral	Moderate	Neutral	Moderate	Mild	Moderate	Neutral	Neutral	Neutral	Moderate
CHF	Neutral	Neutral	Neutral	Moderate	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
CVD	Benefit			Neutral			Safe	?			
BONE	Neutral	Neutral	Neutral	Moderate Bone Loss	Neutral	Neutral	Neutral	Neutral	Neutral	? Bone Loss	Neutral

Few adverse events or possible benefits — Use with caution — Likelihood of adverse effects

INDIVIDUALIZAR

– “no hay enfermedades, sino enfermos”

CVD Risk Factor Modifications Algorithm

DYSLIPIDEMIA

THERAPEUTIC LIFESTYLE CHANGES *(See Obesity Algorithm)*

LIPID PANEL: Assess CVD Risk

Statin Therapy

If TG > 500 mg/dL, fibrates, omega-3 ethyl esters, niacin

If statin-intolerant

Try alternate statin, lower statin dose or frequency, or add nonstatin LDL-C-lowering therapies → Repeat lipid panel; assess adequacy, tolerance of therapy → Intensify therapies to attain goals according to risk levels

RISK LEVELS	MODERATE DM but no other major risk and/or age <40	HIGH DM + major CVD risk(s) (HTN, Fam Hx, low HDL-C, smoking) or CVD*
	DESIRABLE LEVELS	DESIRABLE LEVELS
LDL-C (mg/dL)	<100	<70
Non-HDL-C (mg/dL)	<130	<100
TG (mg/dL)	<150	<150
TC/HDL-C	<3.5	<3.0
Apo B (mg/dL)	<90	<80
LDL-P (nmol/L)	<1200	<1000

If not at desirable levels: Intensify TLC (weight loss, physical activity, dietary changes) and glycemic control; Consider additional therapy

To lower LDL-C: Intensify statin, add ezetimibe &/or colesevelam &/or niacin
To lower Non-HDL-C, TG: Intensify statin &/or add OM3EE &/or fibrates &/or niacin
To lower Apo B, LDL-P: Intensify statin &/or ezetimibe &/or colesevelam &/or niacin

Assess adequacy & tolerance of therapy with focused laboratory evaluations and patient follow-up

* even more intensive therapy might be warranted

HYPERTENSION

GOAL: SYSTOLIC ~130, DIASTOLIC ~80 mm Hg

ACEi or ARB

For initial blood pressure >150/100 mm Hg: Dual therapy

ACEi or ARB + Thiazide ✓ / Calcium Channel Blocker ✓ / ß-blocker ✓

If not at goal (2–3 months)

Add ß-blocker or calcium channel blocker or thiazide diuretic

If not at goal (2–3 months)

Add next agent from the above group, repeat

If not at goal (2–3 months)

Additional choices (α-blockers, central agents, vasodilators, spironolactone)

Achievement of target blood pressure is critical

Diabetes in Older Adults: A Consensus Report

M. Sue Kirkman, MD,[a] Vanessa Jones Briscoe, PhD, NP, CDE,[b] Nathaniel Clark, MD, MS, RD,[c] Hermes Florez, MD, MPH, PhD,[d] Linda B. Haas, PHC, RN, CDE,[e] Jeffrey B. Halter, MD,[f] Elbert S. Huang, MD, MPH,[g] Mary T. Korytkowski, MD,[h] Medha N. Munshi, MD,[i] Peggy Soule Odegard, BS, PharmD, CDE,[j] Richard E. Pratley, MD,[k] and Carrie S. Swift, MS, RD, BC-ADM, CDE[l]

Patient Characteristics/ Health Status	Rationale	Reasonable A1C Goal (A Lower Goal May Be Set for an Individual if Achievable without Recurrent or Severe Hypoglycemia or Undue Treatment Burden)	Fasting or Preprandial Glucose (mg/dL)	Bedtime Glucose (mg/dL)	Blood Pressure (mmHg)	Lipids
Healthy (Few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5%	90–130	90–150	<140/80	Statin unless contraindicated or not tolerated
Complex/intermediate (Multiple coexisting chronic illnesses[a] or 2+ instrumental ADL impairments or mild to moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90–150	100–180	<140/80	Statin unless contraindicated or not tolerated
Very complex/poor health (Long-term care or end-stage chronic illnesses[b] or moderate to severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%[c]	100–180	110–200	<150/90	Consider likelihood of benefit with statin (secondary prevention more so than primary)

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Pharmacotherapy

- **Considering polypharmacy. Avoid glyburide. Metformin** can be used safely and is the preferred initial therapy in many older adults with type 2 diabetes, but at reduced dose in those with stage III chronic kidney disease, and avoid in those with stage IV or worse. **Assess renal function using eGFR**, not serum creatinine alone.
- **Assess patients for hypoglycemia** regularly by asking the patient and caregiver about symptoms or signs and reviewing blood glucose logs. In type 2 diabetic patients, hypoglycemia risk is linked more to treatment strategies than to achieved lower A1C.
- If recurrent or severe hypoglycemia occurs, strongly consider changing therapy and/or targets.
- Assess the burden of treatment on older adult patients (caregivers), consider patient/caregiver preferences, and attempt to **reduce treatment complexity**.

Meta-Analysis: Glycosylated Hemoglobin and Cardiovascular Disease in Diabetes Mellitus

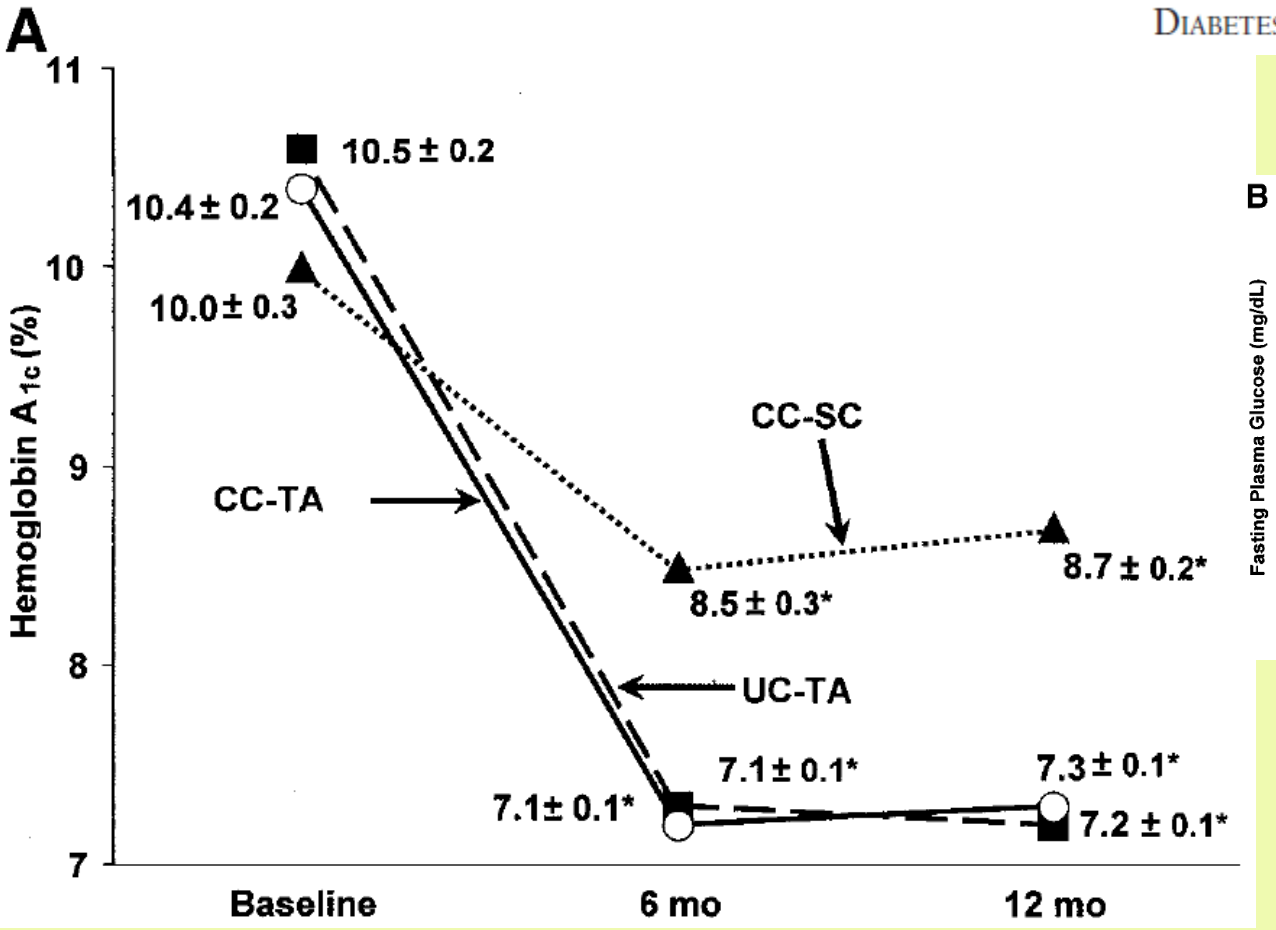
Ann Intern Med. 2004;141(6):421-431

Association of HbA_{1c} levels with vascular complications and death in patients with type 2 diabetes: evidence of glycaemic thresholds

Diabetologia (2012) 55:636–643

Improving Efficacy of Diabetes Management Using Treatment Algorithms in a Mainly Hispanic Population

DIABETES CARE, VOLUME 27, NUMBER 7, JULY 2004



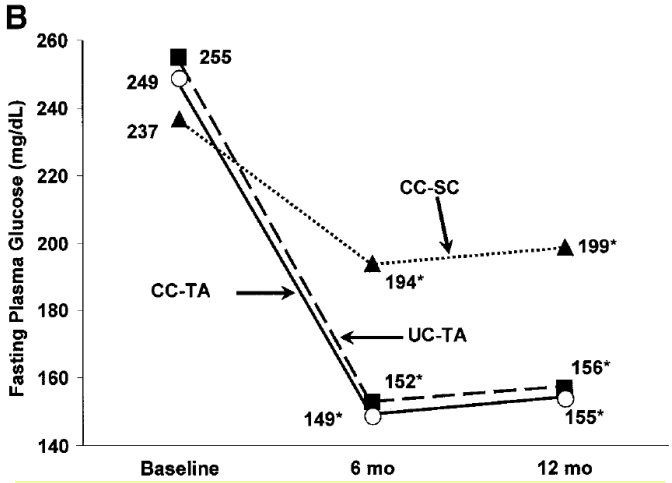


Figure 2—*Effect of treatment on HbA_{1c} (A) and FPG concentration (B). Decrements in HbA_{1c} and FPG at 6 and 12 months were greater (*P < 0.0001) in the UC-TA and CC-TA groups compared with the CC-SC group.*