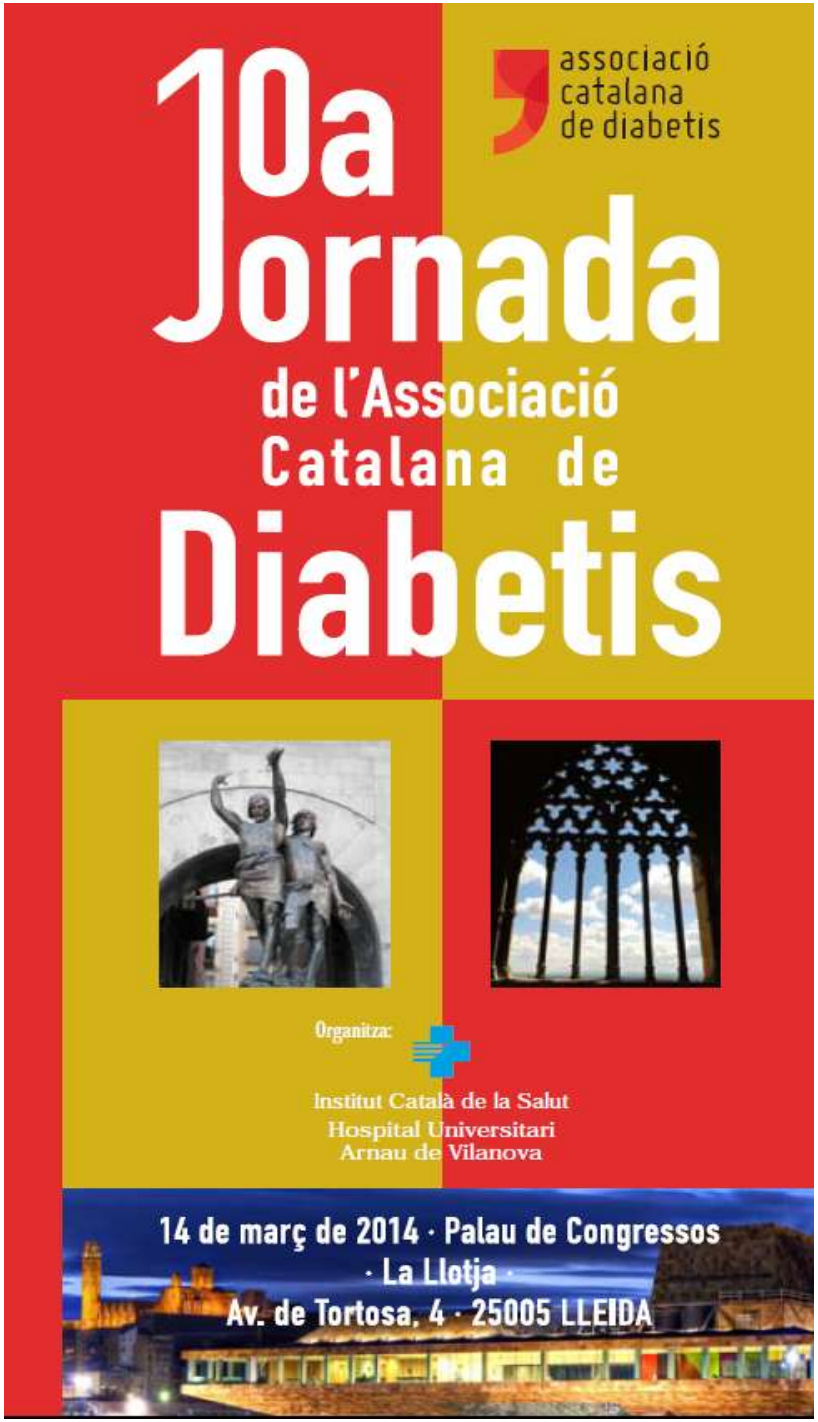

NOUS CONCEPTES PER APRENDRE: FLEXIBILITAT, SETMANAL, POSTPRANDIAL

Dr Manuel Pérez Maraver
Servei d Endocrinologia
Hospital de Bellvitge. IDIBELL

ÍNDEX

Depiction of
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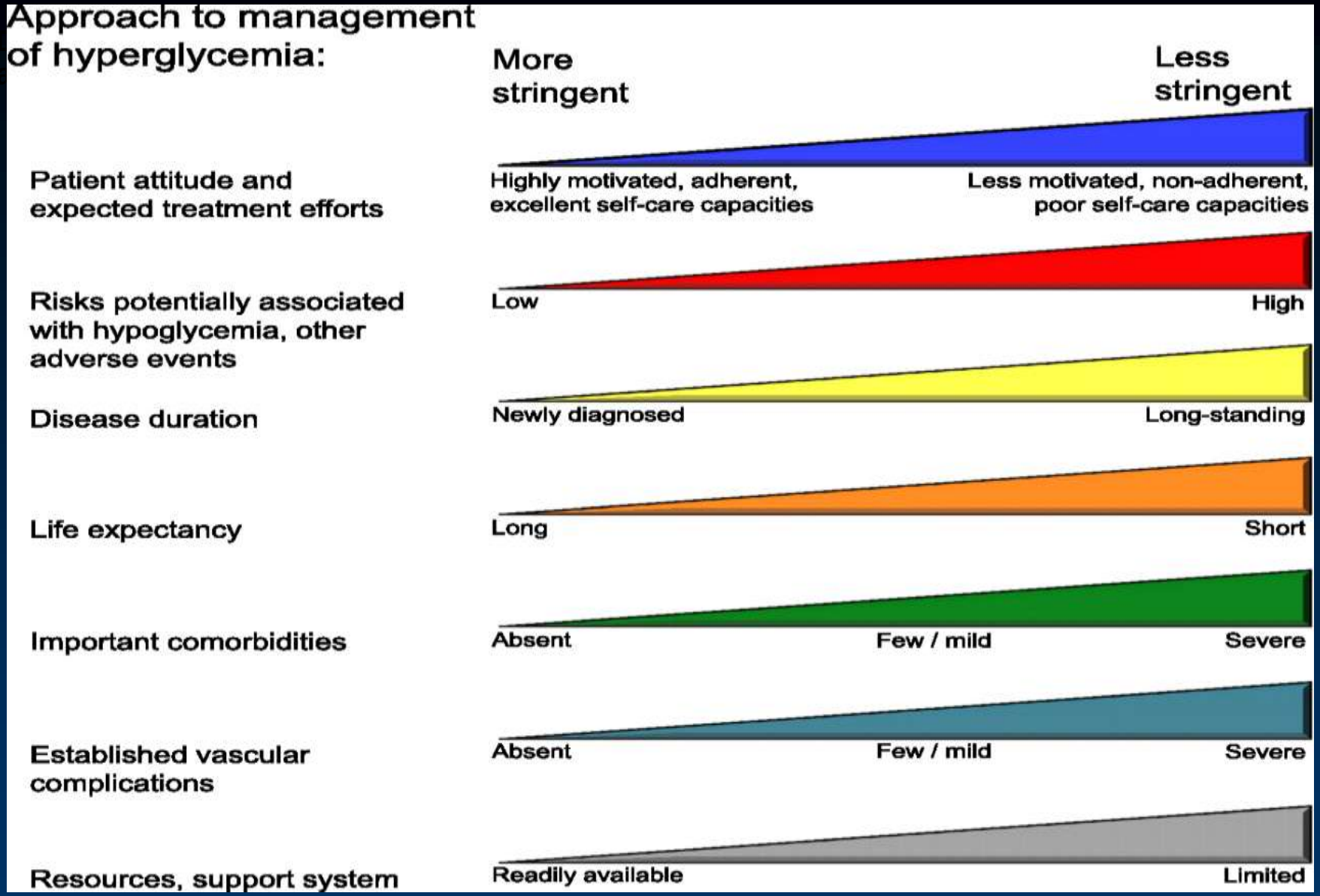

Inzucchi S E et al. Dia Care 2012;35:1364-1379

Conferencia de consenso

Tratamiento de la diabetes tipo 2 en el paciente anciano

Ricardo Gómez Huelgas[a,*], Javier Díez-Espino[b], Francesc Formiga[c], Javier Lafita Tejedor[d], Leocadio Rodríguez Mañas[e], Enrique González-Sarmiento[a], Edelmiro Menéndez[d] y Javier Sangrós[b], en nombre del Grupo de Trabajo para el Documento de Consenso sobre el tratamiento de la diabetes tipo 2 en el anciano[◊]

[a] *Sociedad Española de Medicina Interna (SEMI)*
[b] *Red de Grupos de Estudio de la Diabetes en Atención Primaria de la Salud (redGDPS)*
[c] *Sociedad Española de Geriatría y Gerontología (SEGG)*
[d] *Sociedad Española de Diabetes (SED)*
[e] *Sociedad Española de Medicina Geriátrica (SEMEG)*

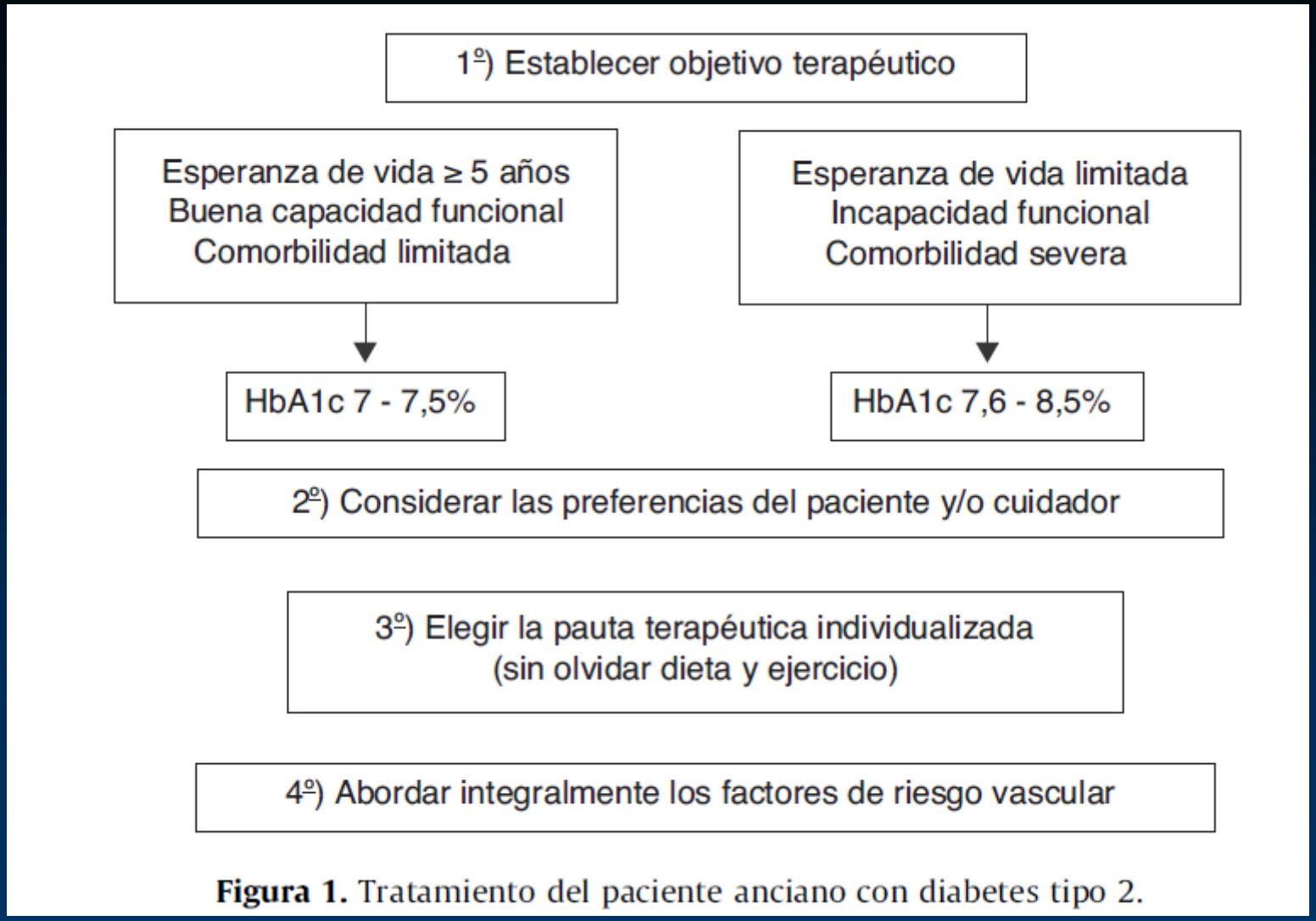

Figura 1. Tratamiento del paciente anciano con diabetes tipo 2.

Medicina Clinica 2012

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

◄ Previous Volume 360:129-139 January 8, 2009 Number 2 Next ►

Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes

William Duckworth, M.D., Carlos Abraira, M.D., Thomas Moritz, M.S., Domenic Reda, Ph.D., Nicholas Emanuele, M.D., Peter D. Reaven, M.D., Franklin J. Zieve, M.D., Ph.D., Jennifer Marks, M.D., Stephen N. Davis, M.D., Rodney Hayward, M.D., Stuart R. Warren, J.D., Pharm.D., Steven Goldman, M.D., Madeline McCarren, Ph.D., M.P.H., Mary Ellen Vitek, William G. Henderson, Ph.D., Grant D. Huang, M.P.H., Ph.D., for the VADT Investigators

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Effects of Intensive Glucose Lowering in Type 2 Diabetes

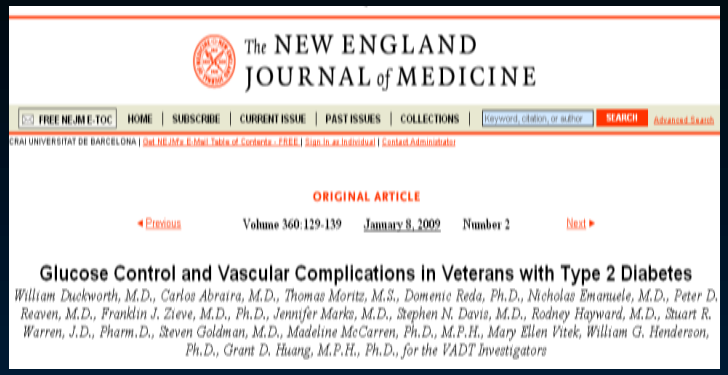
The Action to Control Cardiovascular Risk in Diabetes Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

The ADVANCE Collaborative Group*



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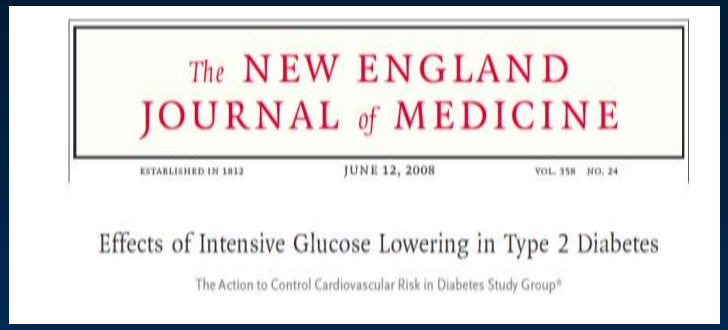

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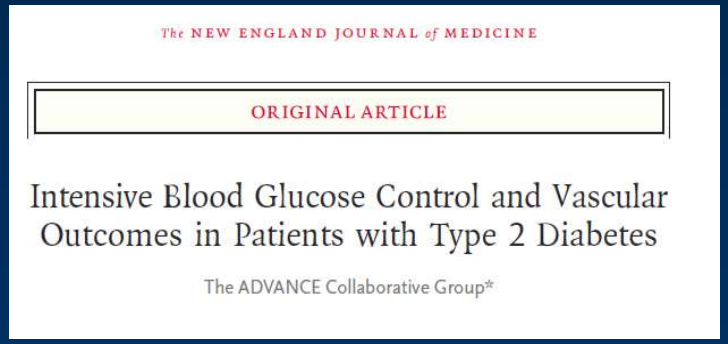


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

The ADVANCE Collaborative Group*

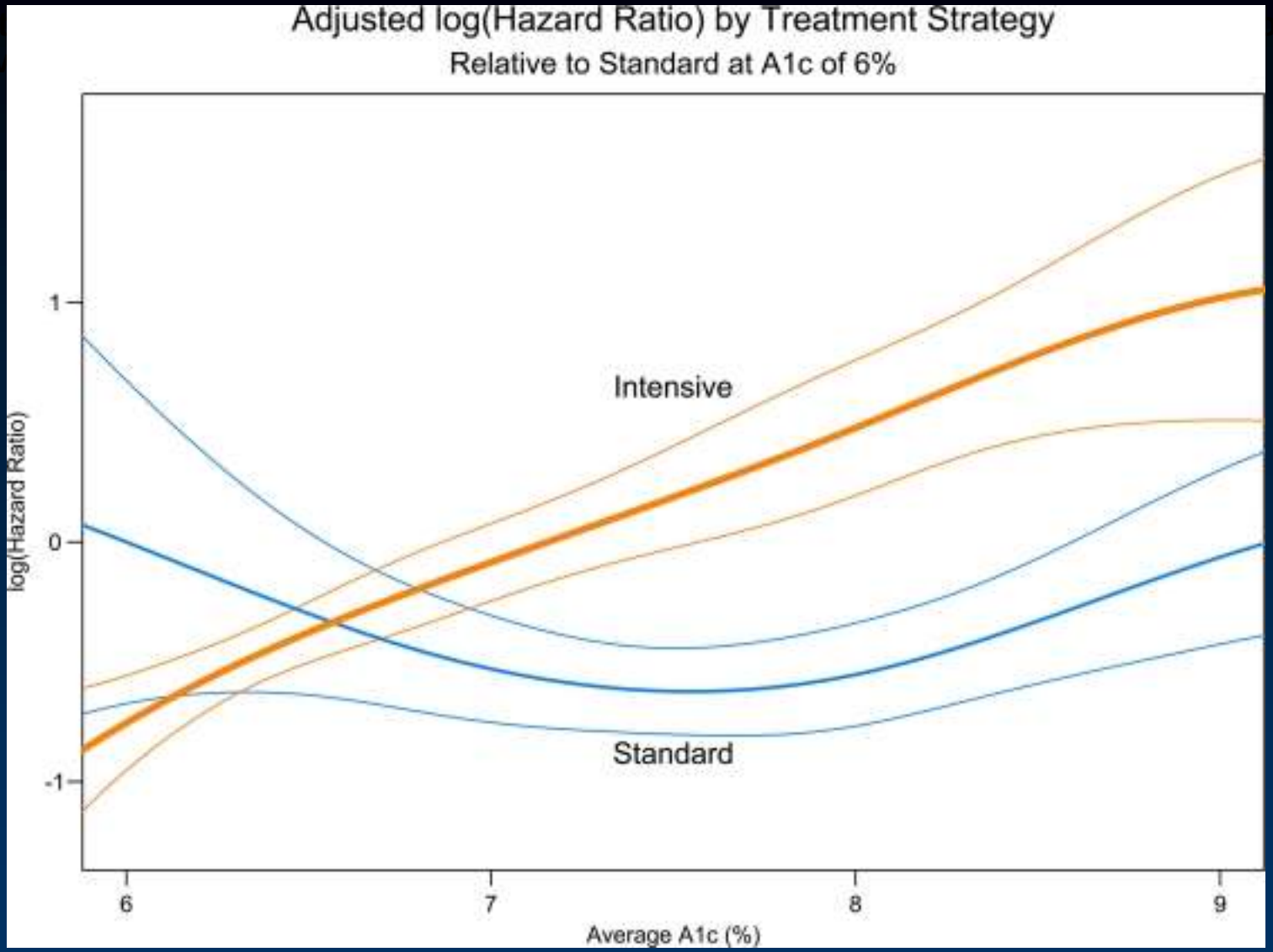
N	Duracion DM	seguim.	HbA1c
1791	11,5 a	5,6 a	9,4% 8,4 vs 6,9
10.251	10,0 a	3,5 a	8,3% 7,5 vs 6,4
11.140	8,0 a	5,0 a	7,5% 7,2 vs 6,5

NO BENEFICIO MACRO NI MICROVASCULAR

SUSPENSION PREMATURA POR ↑ MORTALIDAD

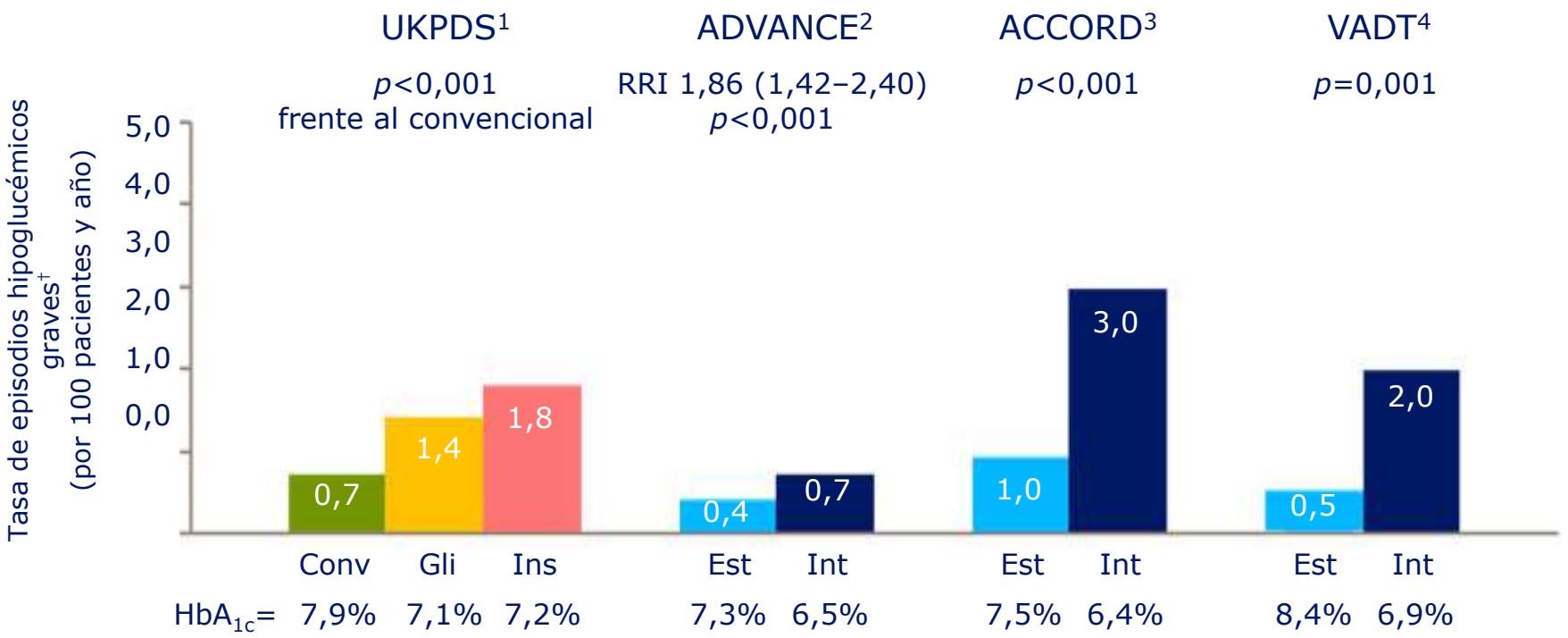
NO BENEFICIO CV NI RTP, SOLO EN NEFROPATÍA

EL UKPDS INTENSIFICA A LOS PACIENTES DESDE EL DX



Riddle et al. Diabetes Care 2010; 33: 983-90

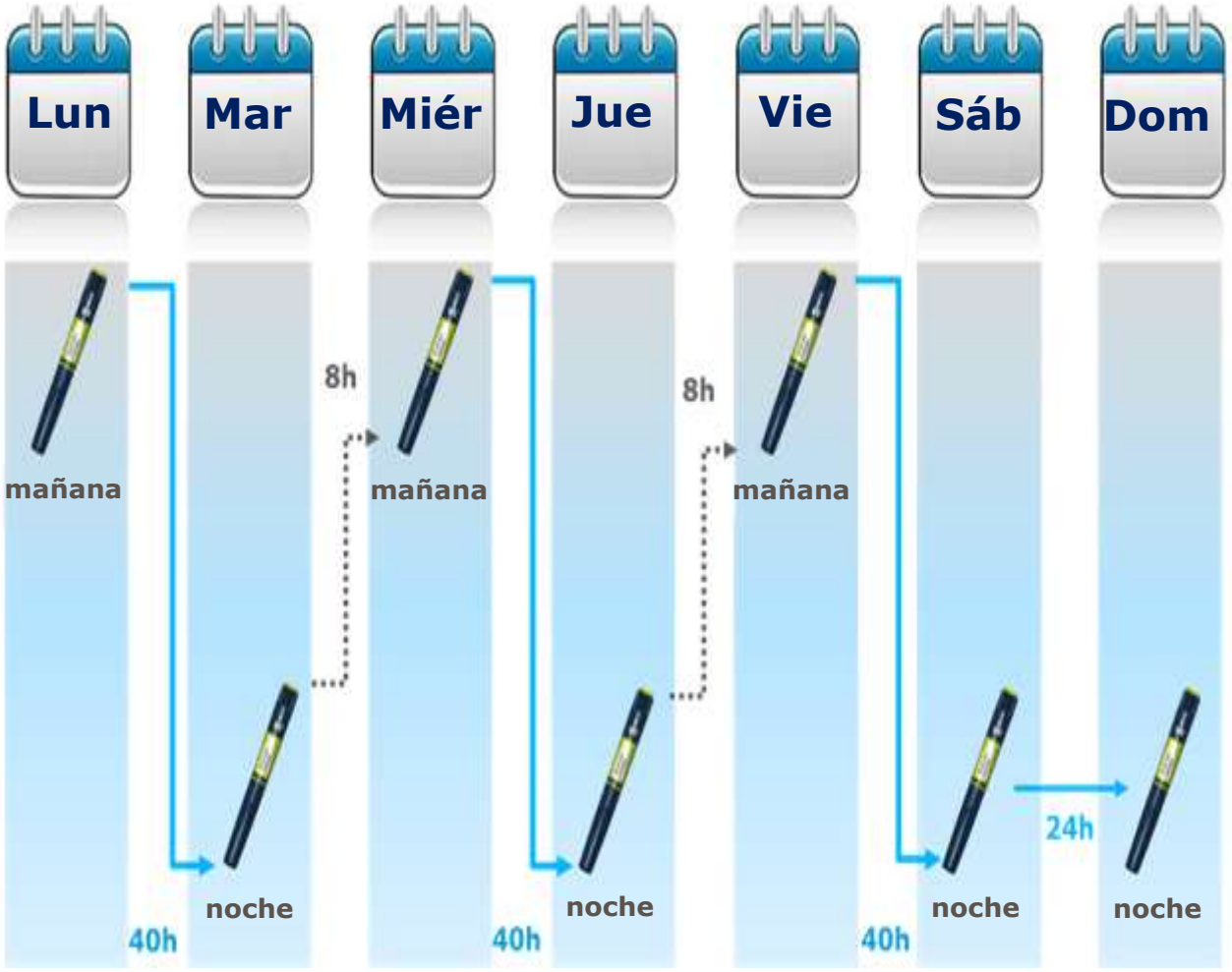
Mayor tasa de hipoglucemias graves con el control intensivo de la glucemia*



*El control intensivo de la glucemia se definió de maneras diferentes en estos ensayos
†Hipoglucemia necesitada de cualquier asistencia en los ensayos de hipoglucemiantes
conv, tratamiento convencional; gli, glibenclamida; RRI, razón de riesgos instantáneos, ins, insulina; int, tratamiento intensivo; est, tratamiento estándar

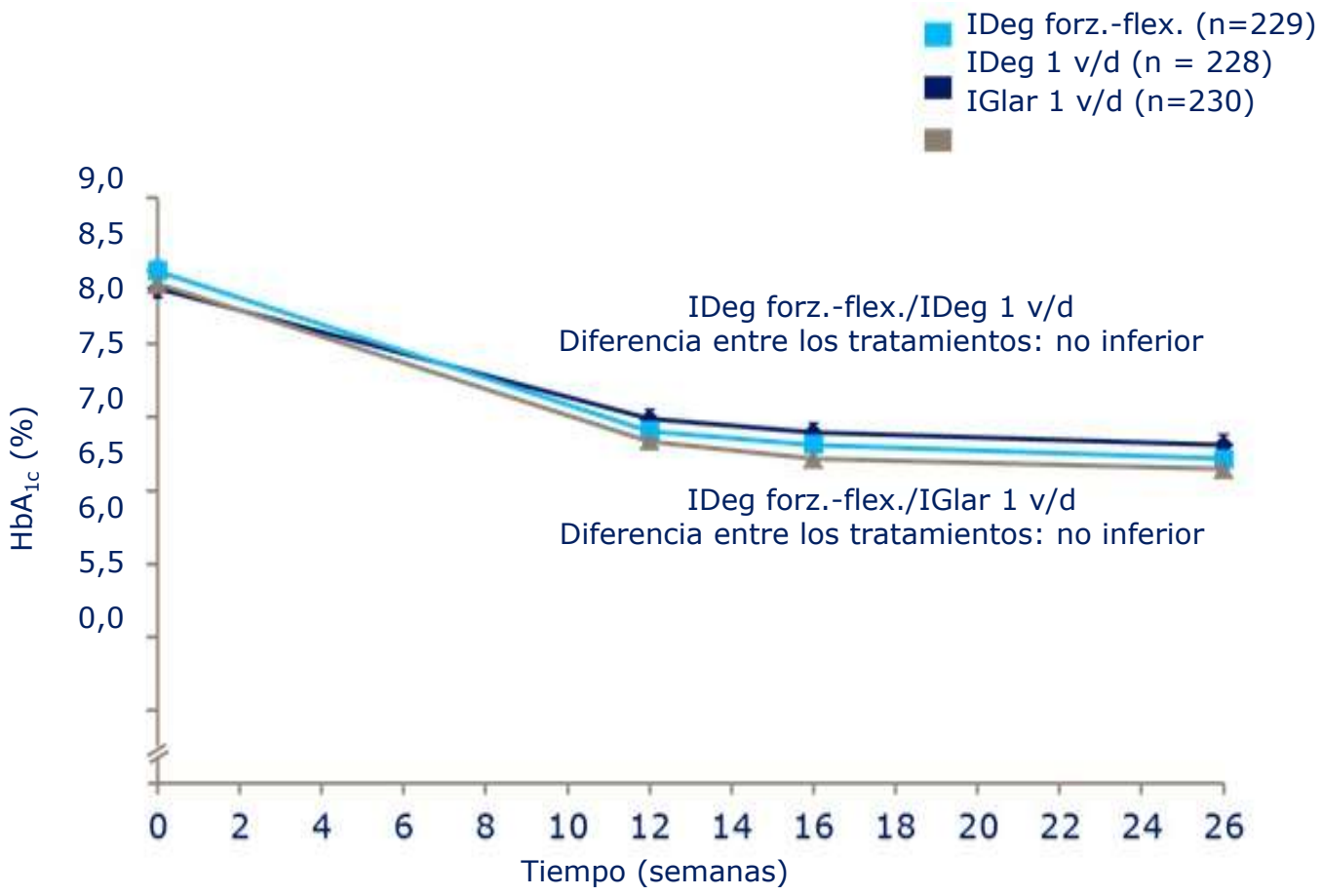
1. UKPDS Group. *Lancet* 1998;352:837–53; 2. Patel *et al;* ADVANCE Collaborative Group. *N Engl J Med* 2008;358:2560–72;
3. Gerstein *et al*; ACCORD Group. *N Engl J Med* 2008;358:2545–59; 4. Duckworth *et al. N Engl J Med* 2009;360:129–39

Grupo con pauta flexible de insulina
Forzando la posología flexible en los casos extremos



Meneghini *et al. Diabetes Care* 2013;36: 858-64
Mathieu et al. J Clin Endocrinol Metab. 2013; 98: 1154-62

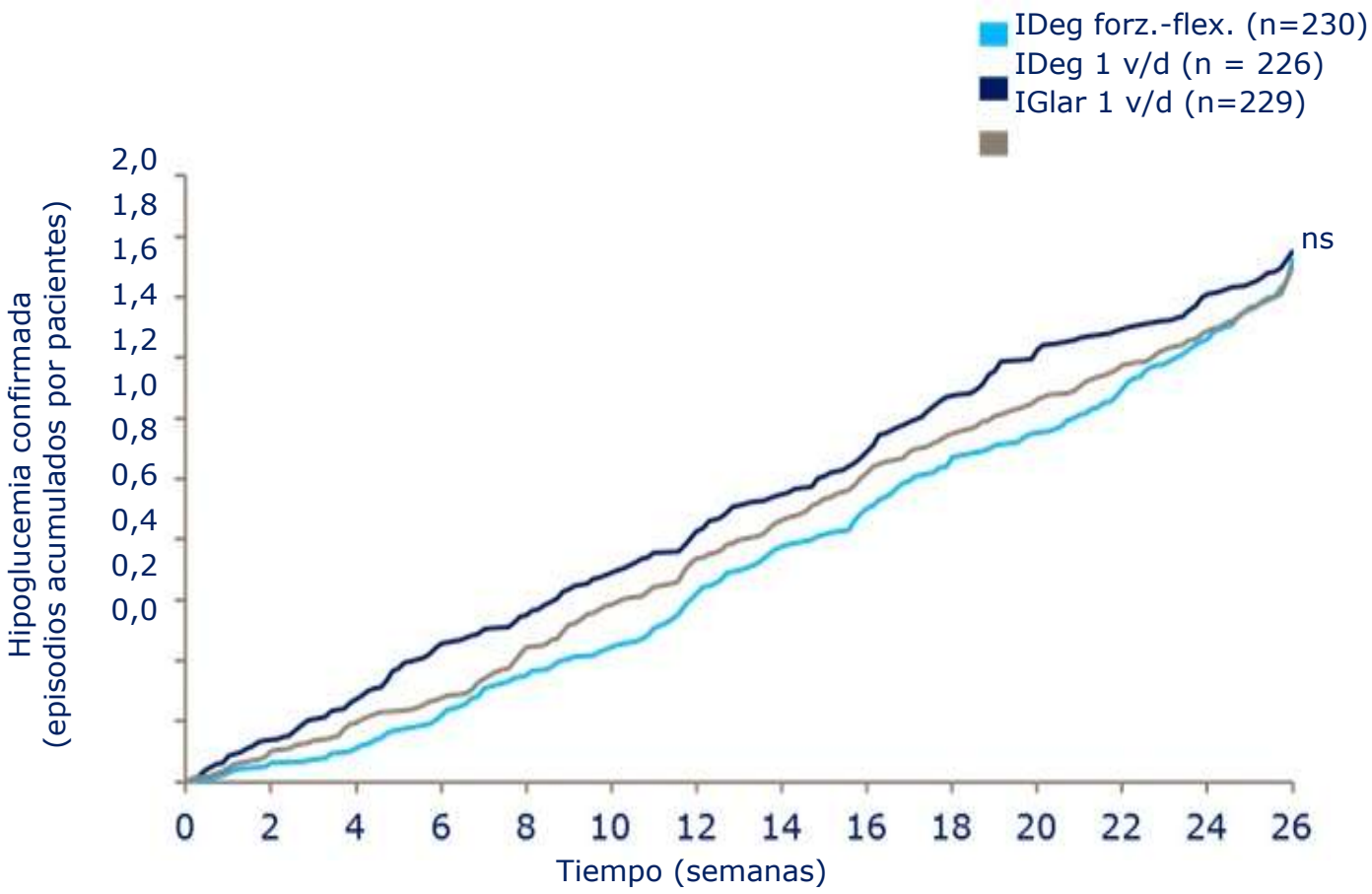
BEGIN® Flex–DM2
HbA_{1c}



Media±EEM; CAC; LOCF
Comparaciones: cálculos ajustados para múltiples covariables

Birkeland *et al.* IDF 2011:P-1443; Bain *et al.* IDF 2011:O-0508; Birkeland *et al. Diabetologia* 2011;54(Suppl. 1):S423; Atkin *et al. Diabetologia* 2011;54(Suppl. 1):S53; Meneghini *et al. Diabetes* 2011;60(Suppl. 1A):LB10

BEGIN® Flex – DM2
hipoglucemia confirmada



GAS
Comparaciones: cálculos ajustados para múltiples covariables

Birkeland *et al.* IDF 2011:P-1443; Bain *et al.* IDF 2011:O-0508; Birkeland *et al. Diabetologia* 2011;54(Suppl. 1):S423; Atkin *et al. Diabetologia* 2011;54(Suppl. 1):S53; Meneghini *et al. Diabetes* 2011;60(Suppl. 1A):LB10

Depiction of the elements of decision making used to determine appropriate efforts to a

ORIGINAL ARTICLE

Contributions of Fasting and Postprandial Plasma Glucose Increments to the Overall Diurnal Hyperglycemia of Type 2 Diabetic Patients

Variations with increasing levels of HbA_{1c}

LOUIS MONNIER, MD[1]
HÉLÈNE LAPINSKI, MD[1]
CLAUDE COLETTE, PHD[2]

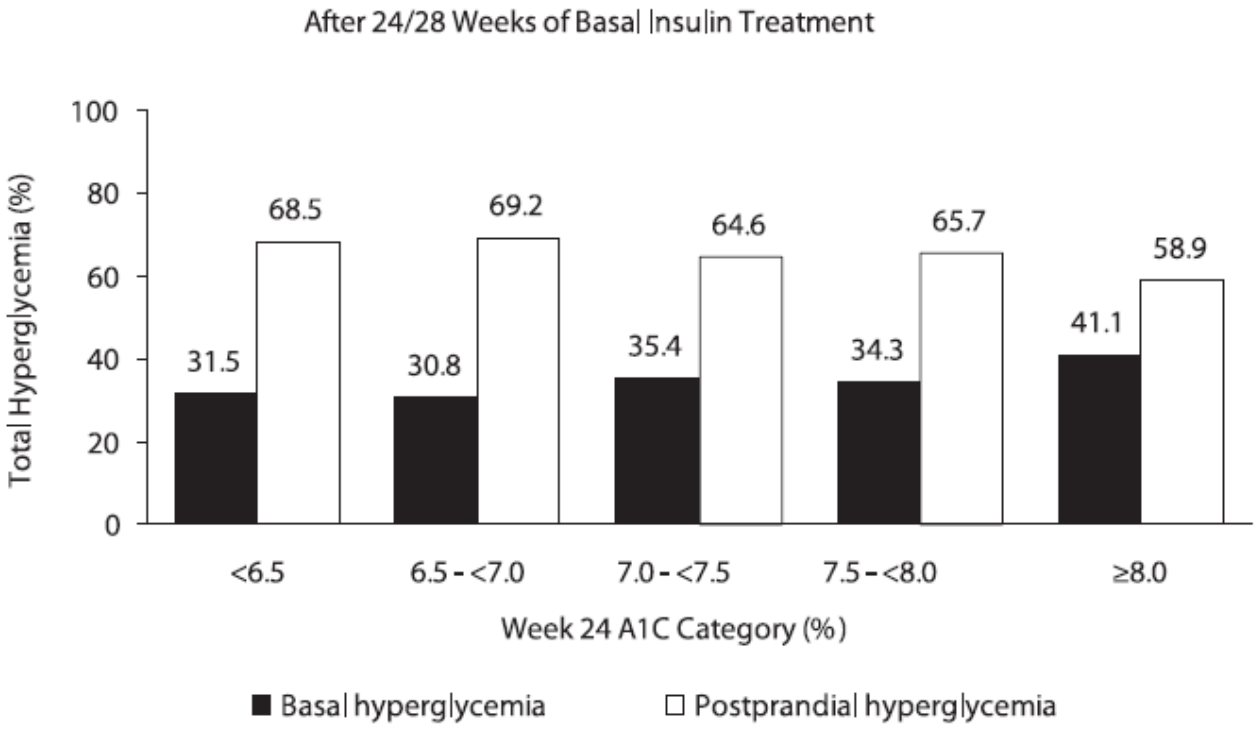
the same type of patients, it has been reported (3) that preprandial PG concentrations were related to HbA_{1c} more strongly than postprandial concentrations. However, a better correlation was observed between HbA_{1c} and mean daily glucose

Monnier L. Diabetes Care 2003

En pacientes tratados con insulina basal, la GPP —no la GA— es el factor que más contribuye a la hiperglucemia

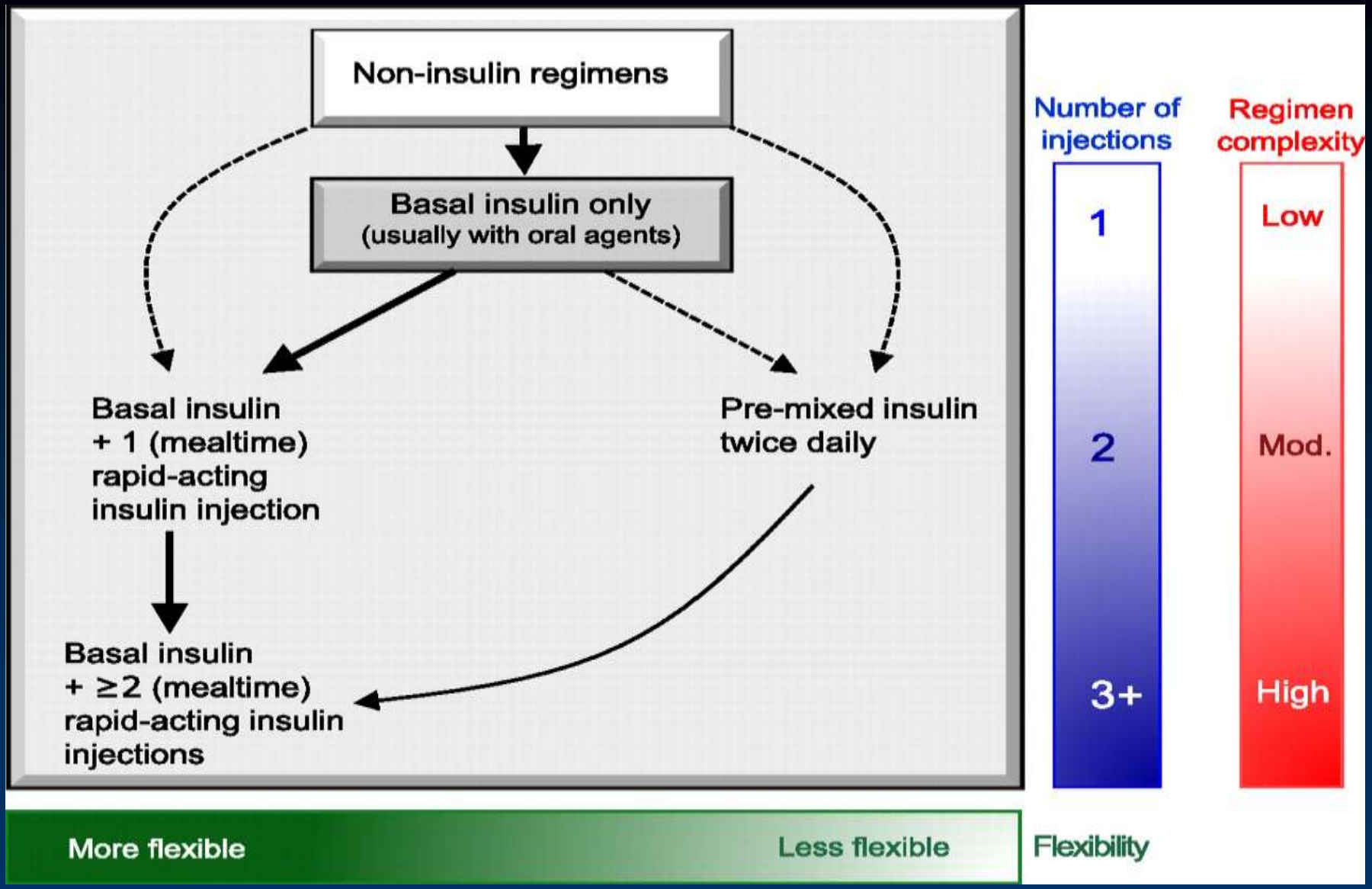
El objetivo de controlar la GPA y la GPP es esencial para obtener resultados clínicos óptimos

Contribución relativa de la hiperglucemia en ayunas y postprandial a la hiperglucemia general en la semana 24/28 en pacientes que reciben insulina basal (N=1261)



Riddle et al. *Diabetes Care* 2011;**34**:2508–14

Datos recopilados de seis ensayos controlados, aleatorizados y de diseño similar, en pacientes con DMT2 mal controlados con ADO



Inzucchi S E et al. Dia Care 2012;35:1364-1379

Addition of Biphasic, Prandial, or Basal Insulin to Oral Therapy in Type 2 Diabetes

Rury R. Holman, M.B., Ch.B., F.R.C.P., Kerensa I. Thorne, M.Sc., Andrew J. Farmer, D.M., F.R.C.G.P., Melanie J. Davies, M.D., F.R.C.P., Joanne F. Keenan, B.A., Sanjoy Paul, Ph.D., and Jonathan C. Levy, M.D., F.R.C.P., for the 4-T Study Group*

ABSTRACT

BACKGROUND

Adding insulin to oral therapy in type 2 diabetes mellitus is customary when glycemic control is suboptimal, though evidence supporting specific insulin regimens is limited.

METHODS

In an open-label, controlled, multicenter trial, we randomly assigned 708 patients with a suboptimal glycated hemoglobin level (7.0 to 10.0%) who were receiving maximally tolerated doses of metformin and sulfonylurea to receive biphasic insulin aspart twice daily, prandial insulin aspart three times daily, or basal insulin detemir once daily (twice if required). Outcome measures at 1 year were the mean glycated hemoglobin level, the proportion of patients with a glycated hemoglobin level of 6.5% or less, the rate of hypoglycemia, and weight gain.

Holman et al. N Engl J Med 2007; 357: 1716-30

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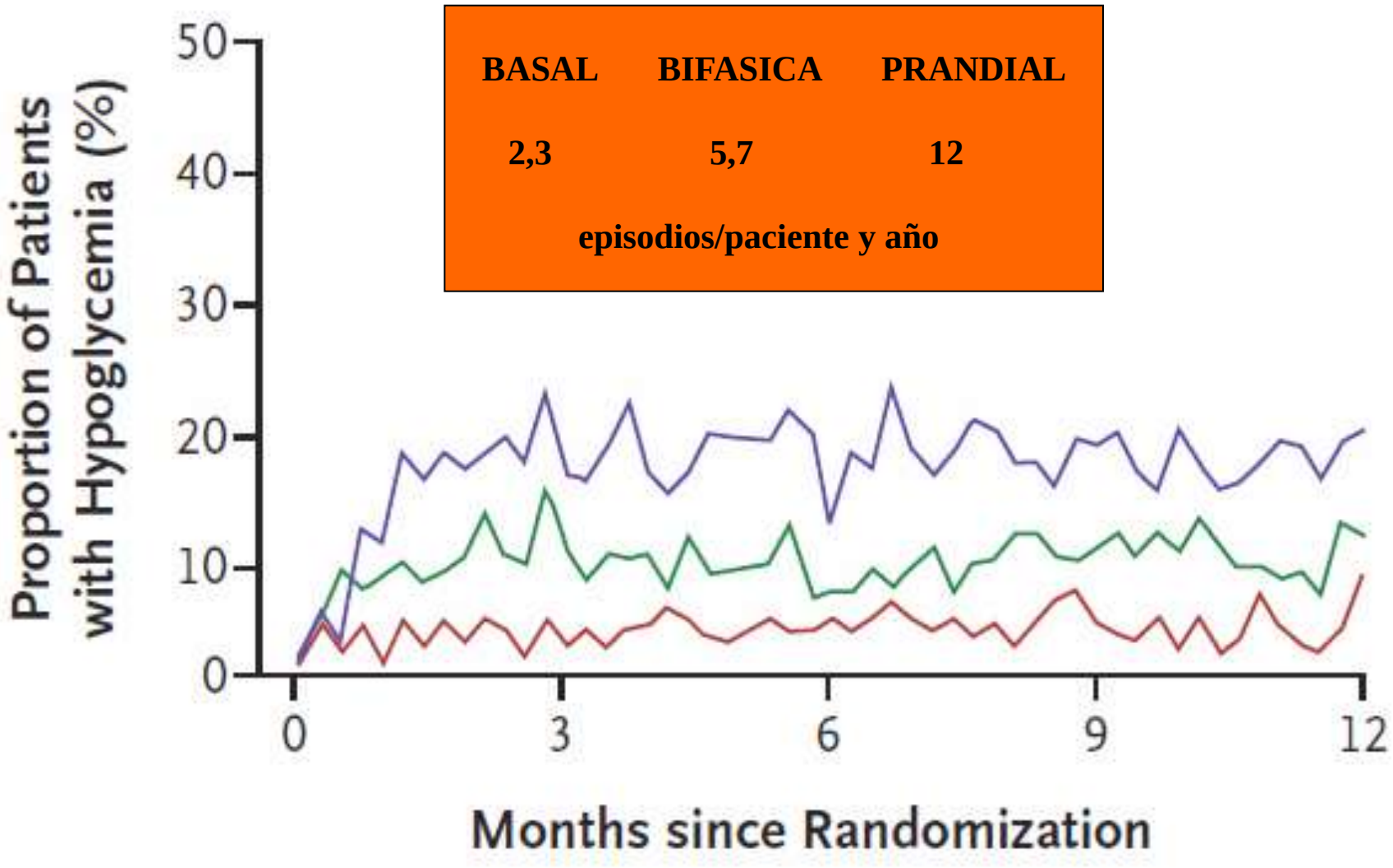


Holman et al. N Engl J Med 2007; 357: 1716-30

SPECIAL ARTICLE

Emergency Hospitalizations for Adverse Drug Events in Older Americans

Daniel S. Budnitz, M.D., M.P.H., Maribeth C. Lovegrove, M.P.H., Nadine Shehab, Pharm.D., M.P.H., and Chesley L. Richards, M.D., M.P.H.

Budnitz et al. N Engl J Med 2011; 365: 2002-12

Table 2. National Estimates of Emergency Hospitalizations for Adverse Drug Events in Older U.S. Adults, According to Therapeutic Category, 2007–2009.*

Therapeutic Category	Annual National Estimate of Hospitalizations (N=99,628)		Proportion of Emergency Department Visits Resulting in Hospitalization
	no.	*% (95% CI)*	%
Hematologic agents	42,104	42.3 (35.5–49.0)	44.6
Endocrine agents	22,726	22.8 (16.7–28.9)	42.1
Cardiovascular agents	9,800	9.8 (7.1–12.5)	42.3
Central nervous system agents	9,621	9.7 (7.6–11.8)	32.2
Antiinfective agents	3,759	3.8 (2.6–4.9)	17.4
Antineoplastic agents	2,882†	2.9 (0.9–4.9)†	51.0
Other agents	3,211	3.2 (2.6–3.8)	15.0
Medications not stated or not known	957	1.0 (0.5–1.5)	20.6
Medications in more than one therapeutic category	4,568†	4.6 (2.7–6.5)	41.2

* Estimates were based on data from the NEISS–CADES project. The proportion of emergency department visits resulting in hospitalization is the ratio of hospitalizations to total emergency department visits for adverse drug events involving the specified therapeutic category.
† The coefficient of variation was greater than 30%.

Budnitz et al. N Engl J Med 2011; 365: 2002-12

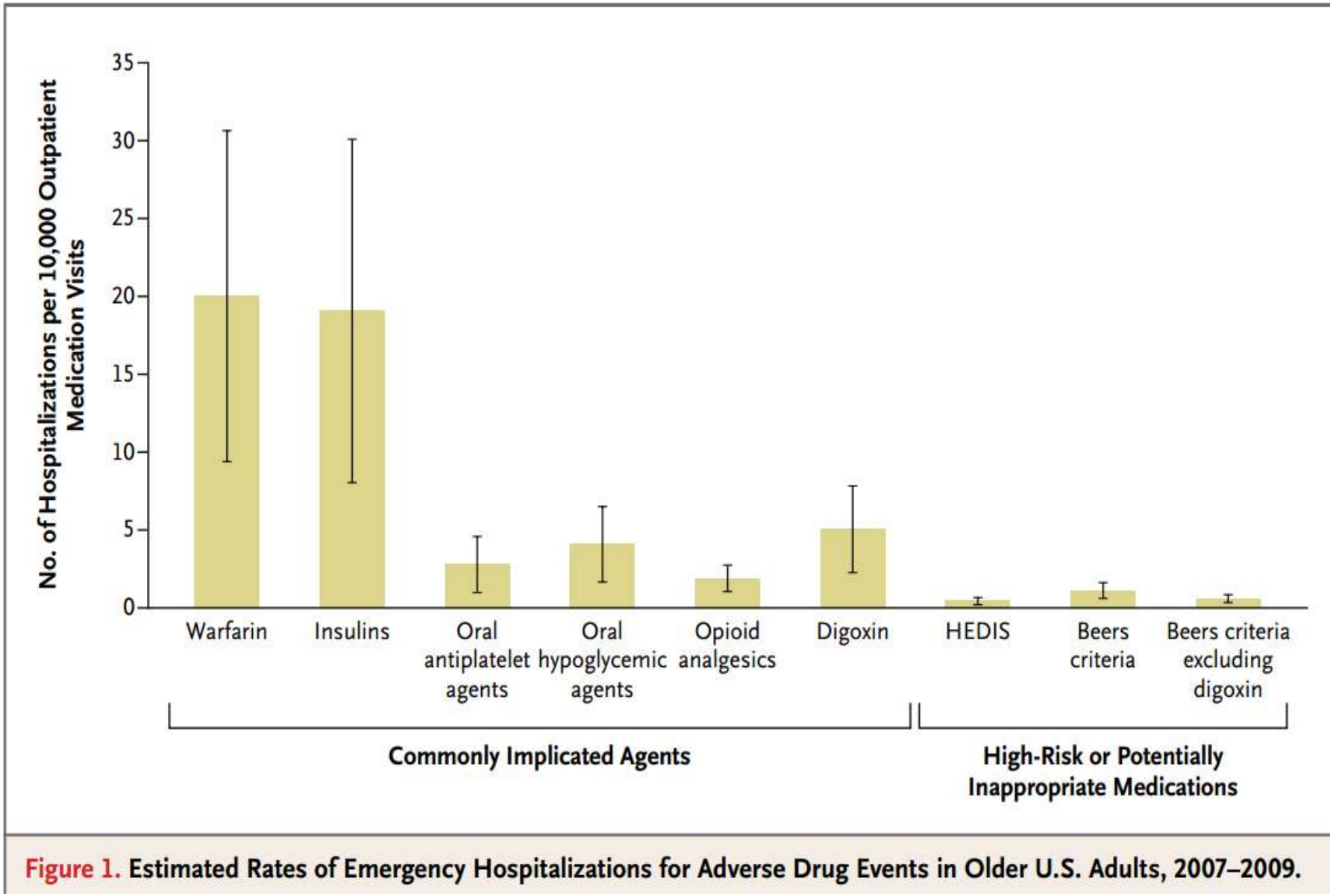
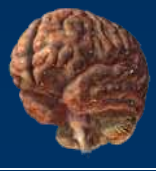


Figure 1. Estimated Rates of Emergency Hospitalizations for Adverse Drug Events in Older U.S. Adults, 2007–2009.

Budnitz et al. N Engl J Med 2011; 365: 2002-12

Accions de les Teràpies Basadas en l´eix incretínic per la DM2: Agonistes del Receptor de GLP-1 i Inhibidors de DPP-4

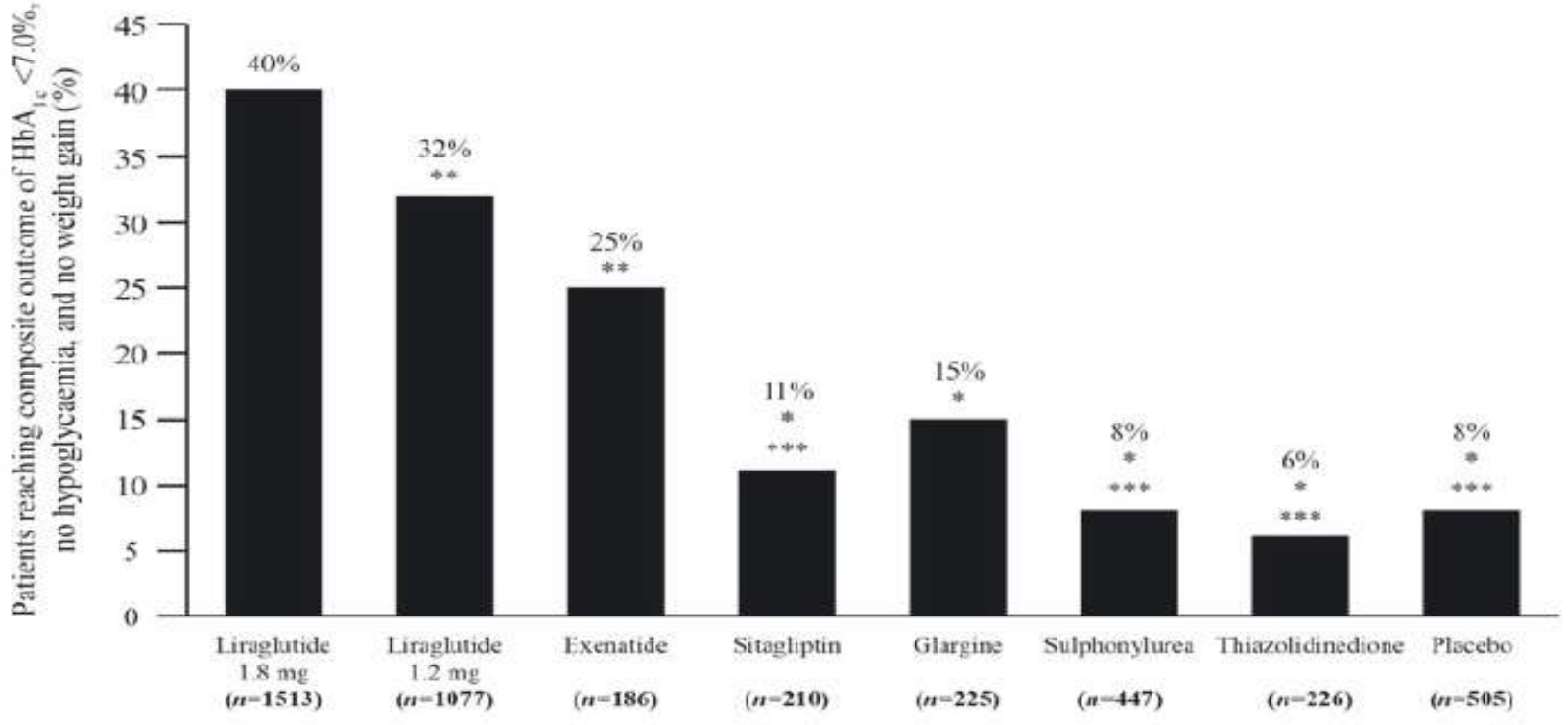


Acció	Agonistes receptor GLP-1[1,2]	Inhibidors DPP-4 [1,2]
↑ Producció Insulina	+++	++
↑ Primera fase resposta insulínica	+++	++
↓ Glucagó	+++	+
Buidat gàstric	Retrasat	Efecte nul
Ingesta	Disminuida	Efecte nul

1. DeFronzo . Curr Med Res Opin. 2008;24(10)2943-2952.; 2. Drucker DJ . Lancet. 2006;368:1696-1705.

Drug/dose	Proportion of patients achieving:				Change from baseline to 26 weeks (LS means, LOCF, ITT)	
	HbA1c <7.0%	HbA1c <7.0%, no weight gain, no hypoglycaemia	HbA1c <7.0%, no weight gain	HbA1c <7.0%, no hypoglycaemia*	HbA1c (%)	Weight (kg)
Liraglutide 1.8 mg	65%	40%	50%	51%	−1.15	−2.27
Liraglutide 1.2 mg	56%	32%	39%	43%	−1.05	−1.69
Sulphonylurea	48%	8%	15%	33%	−0.86	1.65
Thiazolidinedione	34%	6%	9%	23%	−0.54	0.29
Glargine	53%	15%	16%	48%	−0.88	1.14
Exenatide	45%	25%	32%	34%	−0.81	−1.78
Sitagliptin	30%	11%	17%	21%	−0.64	−0.29
Placebo	18%	8%	11%	12%	−0.01	−0.85

ITT, intent to treat; LOCF, last observation carried forward; LS, least squares.
*$p < 0.05$ liraglutide 1.8 mg versus all comparators but glargine.



original article

Diabetes, Obesity and Metabolism 15: 252–257, 2013.

ORIGINAL ARTICLE

Improved glycaemic control with vildagliptin added to insulin, with or without metformin, in patients with type 2 diabetes mellitus

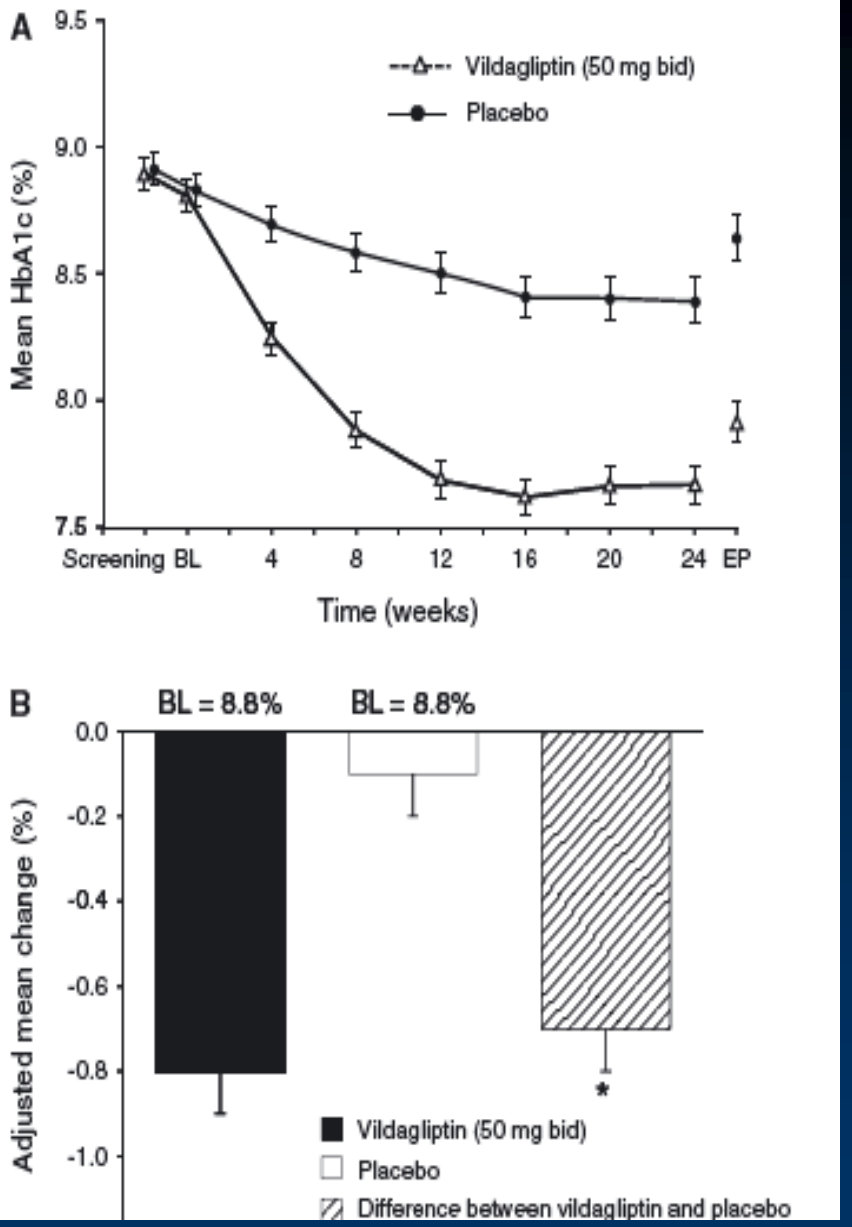
W. Kothny[1], J. Foley[1], P. Kozlovski[2], Q. Shao[1], B. Gallwitz[3] & V. Lukashevich[1]

[1]*Novartis Pharmaceuticals, East Hanover, NJ, USA*
[2]*Novartis Pharma AG, Basel, Switzerland*
[3]*Department of Medicine IV, Eberhard-Karls University Tübingen, Tübingen, Germany*

Kothny et al. Diabet Obes Met 2013; 15: 252-7

Table 1. Baseline patient demographic and background characteristics and therapies.

	Vildagliptin 50 mg bid n = 228	Placebo n = 221
Age (year)	59.3 (9.9)	59.1 (10.1)
≥65 years, n (%)	68 (29.8)	67 (30.3)
Gender, female, n (%)	119 (52.2)	106 (48.0)
Race, n (%)		
White	116 (50.9)	116 (52.5)
Asian	87 (38.2)	86 (38.9)
Other	25 (11.0)	19 (8.6)
BMI (kg/m^2)	28.9 (4.4)	29.0 (4.6)
Weight (kg)	77.9 (16.2)	78.9 (16.7)
HbA1c (%)	8.8 (1.0)	8.8 (1.0)
[illegible]	[illegible]	[illegible]
T2DM duration (year)	12.9 (6.9)	13.2 (7.9)
[illegible]	[illegible]	[illegible]
Insulin use at screening, n (%)		
Intermediate-acting	39 (17.1)	35 (15.8)
Long-acting	52 (22.8)	51 (23.1)
Premixed	137 (60.1)	135 (61.1)
Duration of insulin use (year)	4.4 (4.8)	4.5 (5.0)
Daily dose of insulin (IU)	39.9 (18.1)	41.9 (20.4)
Insulin injections/day	1.8 (0.4)	1.8 (0.4)
Metformin use at screening, n (%)		
Yes	139 (61.0)	137 (62.0)
No	89 (39.0)	84 (38.0)



Kothny et al. Diabet Obes Met 2013; 15: 252-7

Annals of Internal Medicine | ORIGINAL RESEARCH

Use of Twice-Daily Exenatide in Basal Insulin–Treated Patients With Type 2 Diabetes

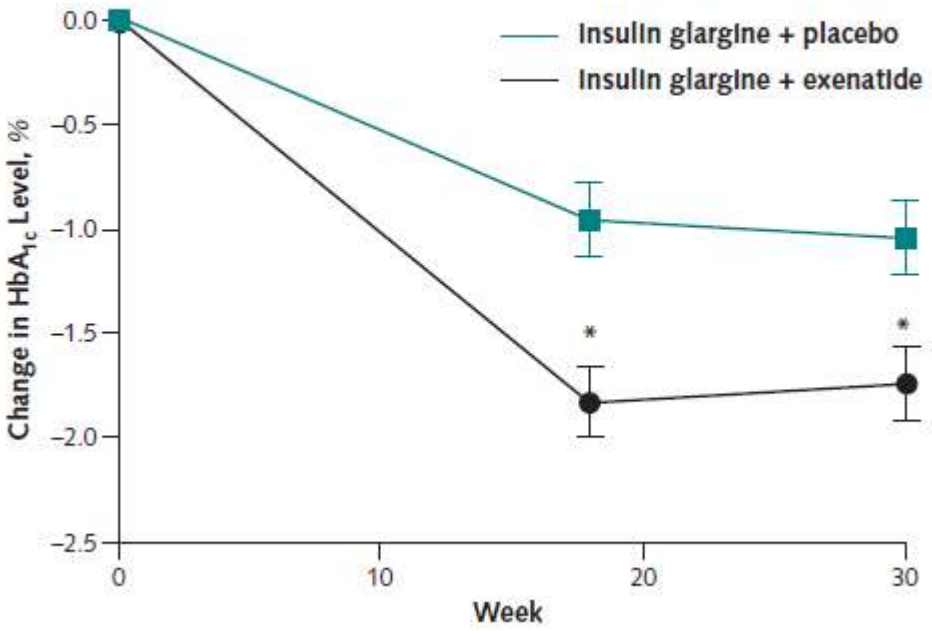
A Randomized, Controlled Trial

John B. Buse, MD, PhD; Richard M. Bergenstal, MD; Leonard C. Glass, MD; Cory R. Heilmann, PhD; Michelle S. Lewis, PhD; Anita Y.M. Kwan, MS; Byron J. Hoogwerf, MD; and Julio Rosenstock, MD

Table 1. Baseline Patient Characteristics*

Variable		
Women, *n (%)*		
Age, *y*		
Race, *n (%)*		
American Indian or Alaskan Native		
Asian		
Black or African American		
Multiple		
White		
Hispanic ethnicity, *n (%)*		
Body weight, *kg*		
Body mass index, kg/m^2		
Waist circumference, *cm*		
HbA_{1c} measures		
HbA_{1c} level, %		
HbA_{1c} level >8.0%, *n (%)*		
HbA_{1c} level ≤8.0%, *n (%)*		
Duration of diabetes		
Total duration, *y*	12 (7)	12 (7)
≥10 years, *n (%)*	87 (64)	75 (62)
≥20 years, *n (%)*	20 (15)	15 (12)

Figure 2. Change in HbA_{1c} over 30 weeks.



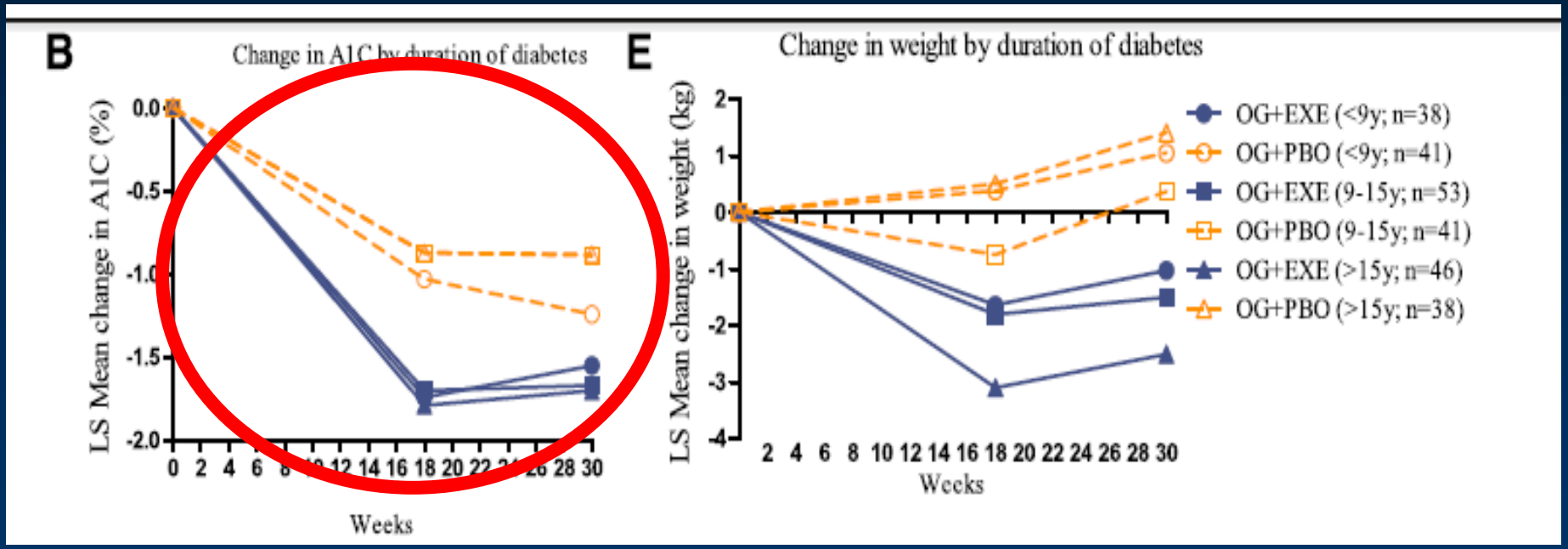
Buse et al. Ann Intern Med 2011; 154: 103-12

Clinical Care/Education/Nutrition/Psychosocial Research
BRIEF REPORT

Baseline Factors Associated With Glycemic Control and Weight Loss When Exenatide Twice Daily Is Added to Optimized Insulin Glargine in Patients With Type 2 Diabetes

JULIO ROSENSTOCK, MD[1]
SYLVIA K. SHENOUDA, PHD[2]
RICHARD M. BERGENSTAL, MD[3]
JOHN B. BUSE, MD, PHD[4]
LEONARD C. GLASS, MD[2]
CORY R. HEILMANN, PHD[2]
ANITA Y.M. KWAN, MS[5]
LEIGH A. MACCONELL, PHD[6]
BYRON JAMES HOOGWERF, MD[5]

and/or pioglitazone, with A1C 7.1–10.5% and BMI ≤45 kg/m^2. At randomization, if A1C >8.0%, insulin glargine dose continued unchanged, but if A1C ≤8.0%, the dose was decreased by 20%. After 5 weeks,



Rosenstock et al. Diabetes Care 2012; 35: 955-8

Efficacy of lixisenatide in patients with different levels of beta cell function as assessed by C-peptide/glucose ratio

J.J. Meier[1], D. Yabe[2], E. Wang[3], J. Lin[4], J. Rosenstock[5], B. Ahrén[6];
[1]Department of Medicine I, St.Josef-Hospital, Bochum, Germany, [2]Division of Diabetes, Clinical Nutrition and Endocrinology, Kansai Electric Power Hospital, Osaka, Japan, [3]Sanofi-Aventis, Bridgewater, [4]Novosys Health, Flemington, [5]Dallas Diabetes and Endocrine Center, Dallas, USA, [6]Lund University, Sweden.

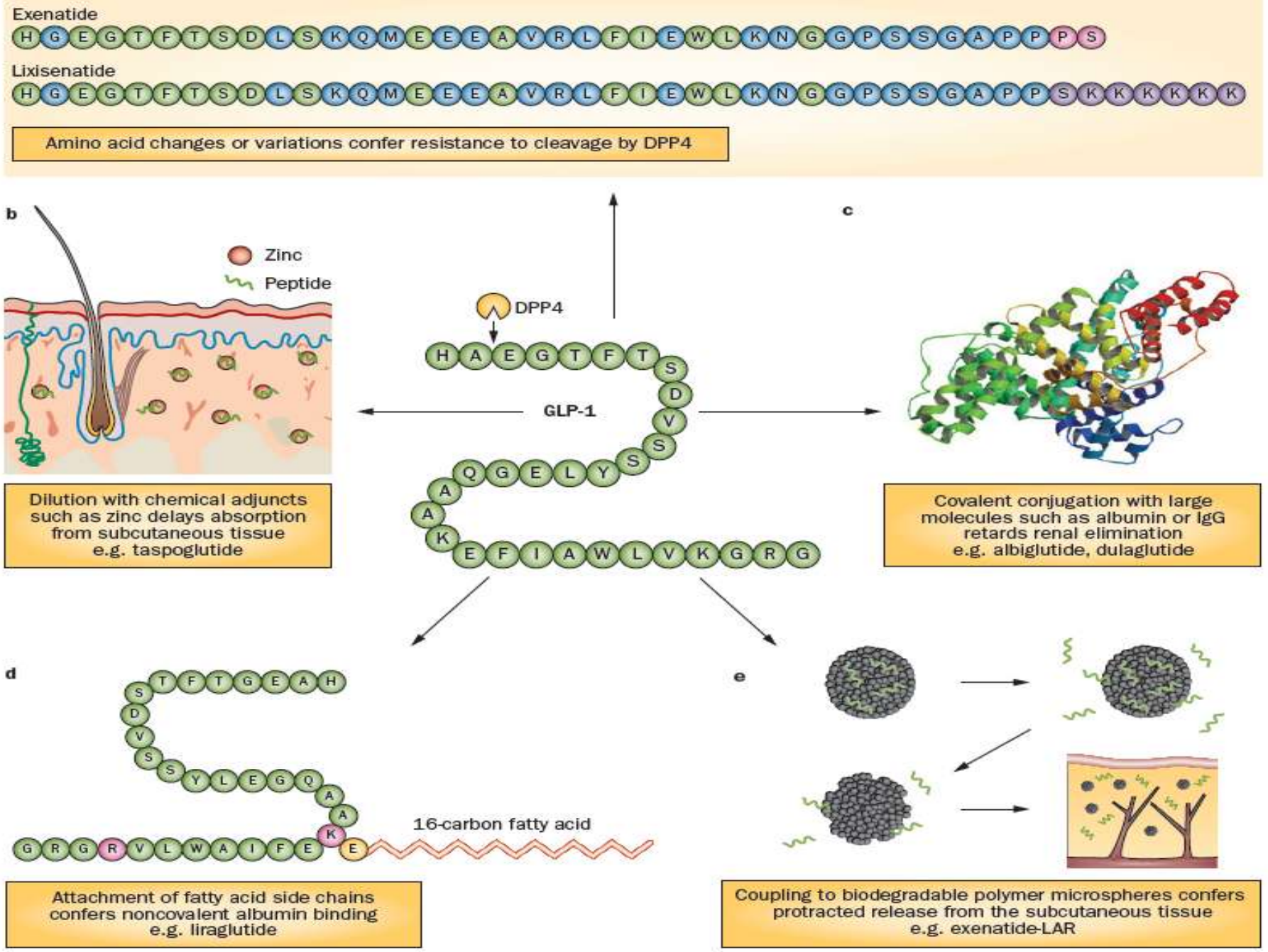
Baseline characteristics and endpoints

	Quartile 1 n=105	Quartile 2 n=115	Quartile 3 n=107	Quartile 4 n=110	p-value
Baseline clinical characteristics					
C-peptide/glucose ratio (nmol/mg), mean (SD)	0.0026 (0.0007)	0.0042 (0.0004)	0.0056 (0.0004)	0.0088 (0.0022)	p<0.0001
Diabetes duration, years (SD)	10.3 (6.3)	8.1 (5.7)	7.2 (5.8)	6.9 (5.7)	p=0.0001
Baseline HbA_{1c} (%), mean (SD)	8.4 (0.8)	8.3 (0.9)	8.1 (0.9)	7.9 (0.9)	p<0.0001
Change from baseline to endpoint					
C-peptide/glucose ratio (nmol/mg), mean (SD)	0.0014 (0.0016)	0.0016 (0.0021)	0.0017 (0.0032)	0.0006 (0.0044)	p=0.0205
HbA_{1c} (%), mean (SD)	-0.9 (0.9)	-1.0 (0.9)	-0.7 (1.0)	-0.9 (0.9)	p=0.0766
FBG (mg/dL), mean (SD)	-15.3 (40.0)	-15.8 (40.0)	-14.6 (41.7)	-20.0 (35.1)	p=0.7392
PPG (mg/dL), mean (SD)*	-135.3 (104.9)	-111.4 (92.4)	-85.0 (95.6)	-86.7 (77.2)	p=0.0001
Symptomatic hypoglycaemia (<60 mg/mL), %	13.3	10.4	12.2	3.6	p=0.0750

SD=standard deviation; HbA_{1c}=glycated haemoglobin; FBG=fasting blood glucose; PPG=postprandial glucose after standardized meal test; *n=104, 114, 105, 110 for Quartiles 1, 2, 3, 4, respectively

Clinical Trial Registration Number: NCT00712673; NCT00713830
Supported by: Sanofi

	INSULINA BASAL	ANALOGO GLP-1
POTENCIA ↓A1c	1,5-2%	1-2%
R. HIPOGLICEMIA	BAJO	NULO
PERFIL	BASAL	POSTPRANDIAL
PESO	↑ LEVE	DESCENSO
INYECCIONES/D	1-2	≤1-2
“TIRAS DE CONTROL”	POCAS	LAS MISMAS



Meier J, Nat Rev Endocrinol 2012; 8:728-42

Table 1 | Comparison of short-acting versus long-acting GLP-1 receptor agonists

Parameters	Short-acting GLP-1 receptor agonists	Long-acting GLP-1 receptor agonists
Compounds	Exenatide Lixisenatide	Albiglutide Dulaglutide Exenatide-LAR Liraglutide
Half-life	2–5 h	12 h–several days
Effects		
Fasting blood glucose levels	Modest reduction	Strong reduction
Postprandial hyperglycaemia	Strong reduction	Modest reduction
Fasting insulin secretion	Modest stimulation	Strong stimulation
Postprandial insulin secretion	Reduction	Modest stimulation
Glucagon secretion	Reduction	Reduction
Gastric emptying rate	Deceleration	No effect
Blood pressure	Reduction	Reduction
Heart rate	No effect or small increase (0–2 bpm)	Moderate increase (2–5 bpm)
Body weight reduction	1–5 kg	2–5 kg
Induction of nausea	20–50%, attenuates slowly (weeks to many months)	20–40%, attenuates quickly (~4–8 weeks)

Abbreviations: GLP-1, glucagon-like peptide 1; LAR, long-acting release.

Meier J, Nat Rev Endocrinol 2012; 8:728-42

Dos tipos distintos de análogos de GLP-1
Influyen sobre la GA y la GPP en diferentes grados

CONTROVERSIA ACTUAL: EFICACIA EN COMBINACIÓN CON INSULINA:
más datos con cortos (4b, GET GOAL), no estudios comparativos entre cortos y largos

Fineman MS, et al. *Diabetes Obes Metab.* 2012;14(8):675-688.

Depiction of the elements of decision making used to determine appropriate efforts to ach

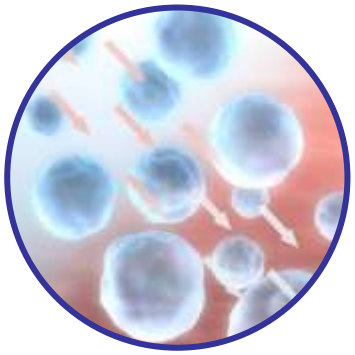
Bydureon: proven microsphere technology provides a continuous level of exenatide

Patented Medisorb® microspheres are a biodegradable polymer that dissipates into CO_2 and water[1]

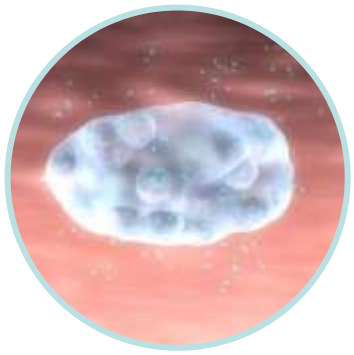
The microspheres deliver a constant presence of exenatide with a single weekly dose[1]

It takes about 2 weeks to achieve concentrations in the therapeutic range[2]

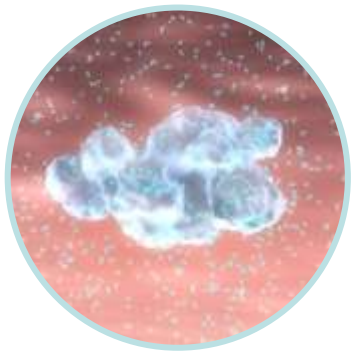
Steady-state exenatide concentration is reached at 6–7 weeks[2]



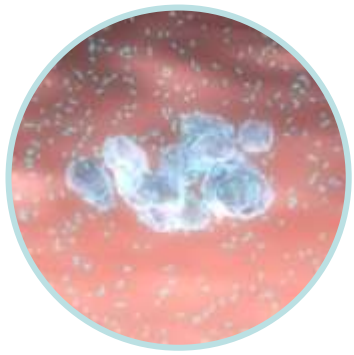
Subcutaneous injection of microsphere suspension of exenatide[1]



Individual microspheres aggregate and initial release of exenatide[1]



Microsphere degradation and continued release of exenatide[1]



Further degradation and metabolism of microsphere polymer provide a sustained level of exenatide[1]

Medisorb® is a registered trademark of Alkermes, Inc.

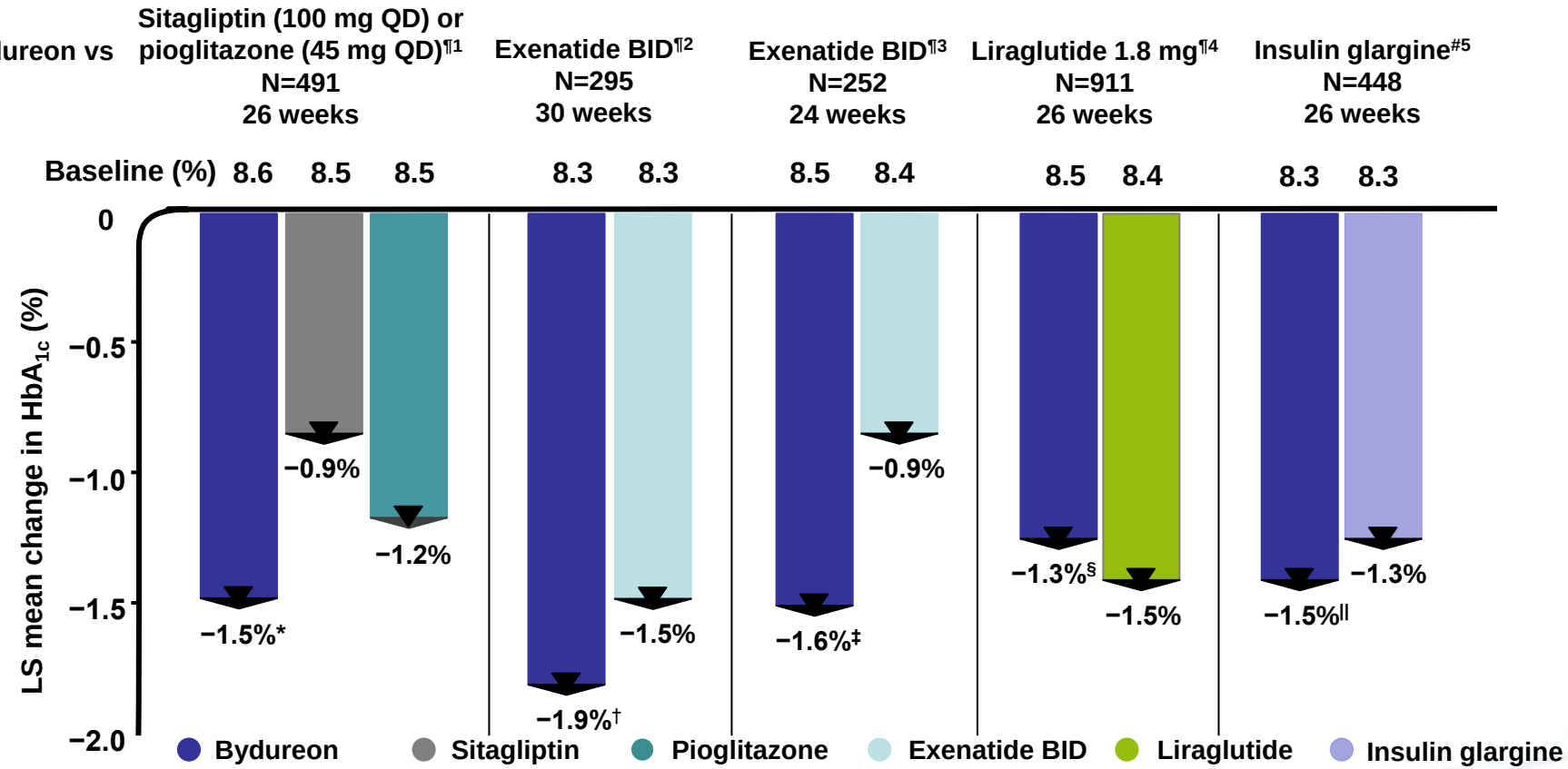
1. DeYoung MB, et al. *Diabetes Technol Ther*. 2011;13:1145-1154; 2. Kim D, et al. *Diabetes Care*. 2007;30:1487-1493.

Bydureon clinical trials

Trial	Comparator	Background	Subjects	Publication
DURATION-1	Exenatide BID Open-label	Drug-naïve, mono and combo failures	295	Drucker, et al. *Lancet.* 2008
DURATION-2	Sitagliptin (100 mg QD) or pioglitazone (45 mg QD) Double-blind	Metformin	491	Bergenstal, et al. *Lancet*. 2010
DURATION-3	Insulin glargine Open-label	Metformin +/- sulphonylurea	456	Diamant, et al. *Lancet*. 2010
DURATION-5	Exenatide BID Open-label	Drug-naïve, mono and combo failures	252	Blevins, et al. *J Clin Endocrin Metab*. 2011
DURATION-6	Liraglutide 1.8 mg Open-label	Mono and combo failures	911	Buse, et al. *Lancet*. 2012

The DURATION-4 clinical trial of Bydureon monotherapy vs metformin, sitagliptin, or pioglitazone monotherapy was conducted in adult patients uncontrolled on diet and exercise alone. Bydureon is not indicated as first-line monotherapy in patients uncontrolled on diet and exercise alone.

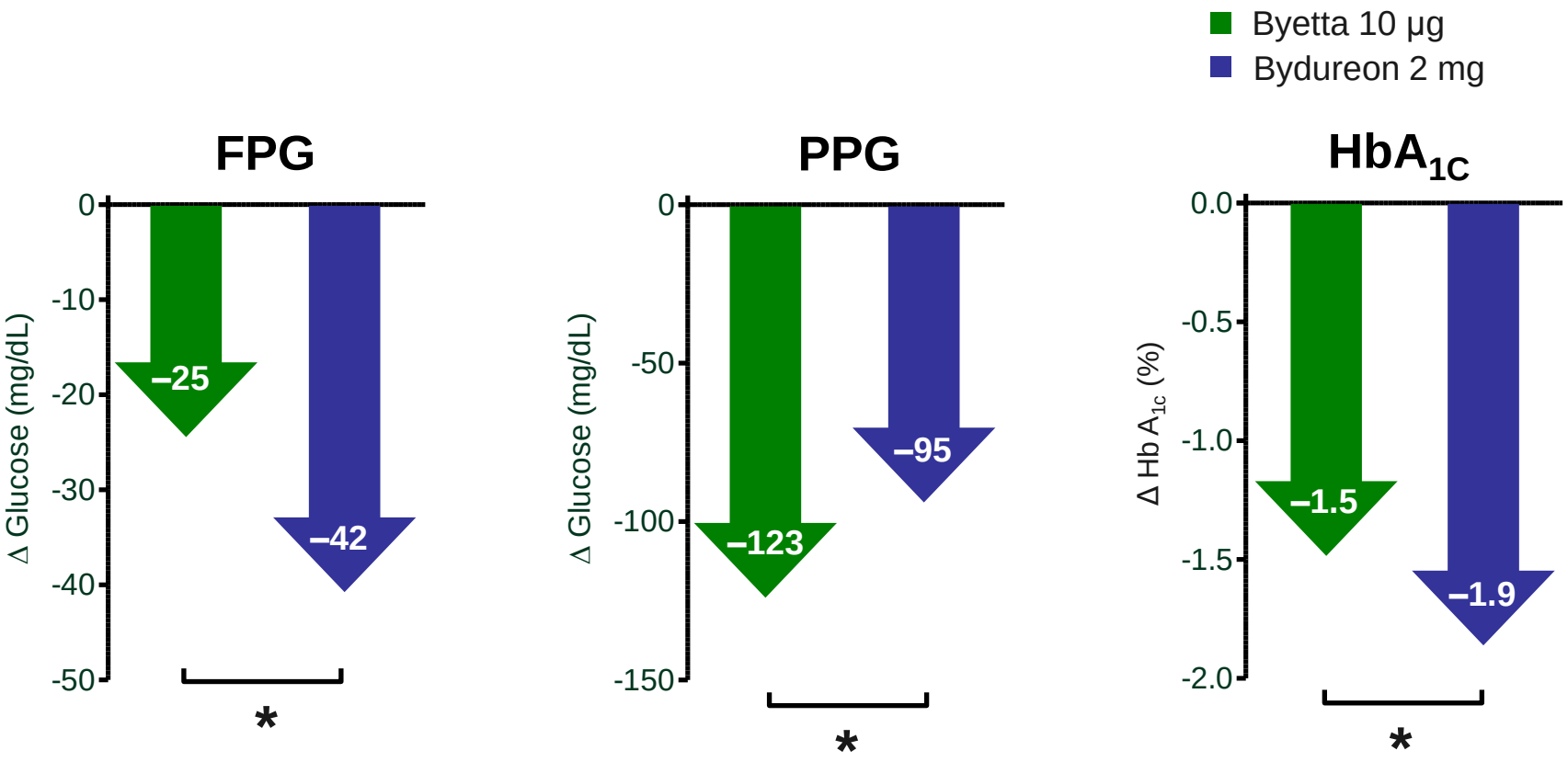
In the DURATION clinical trials, Bydureon demonstrated HbA_{1c} reductions of −1.3% to −1.9%



Data from 24–30 Weeks. *P<0.05 vs both; †P<0.01; ‡P<0.0001; §P=0.02; ‖P=0.017; ¶ITT population; #Modified ITT population.

1. Bergenstal RM, et al. *Lancet*. 2010;376:431-439; 2. Drucker DJ, et al. *Lancet*. 2008;372:1240-1250; 3. Blevins T, et al. *J Clin Endocrin Metab*. 2011;96:1301-1310; 4. Buse JB, et al. *Lancet*. 2013;381(9861):117-124; 5. Diamant M, et al. *Lancet*. 2010;375:2234-2243.

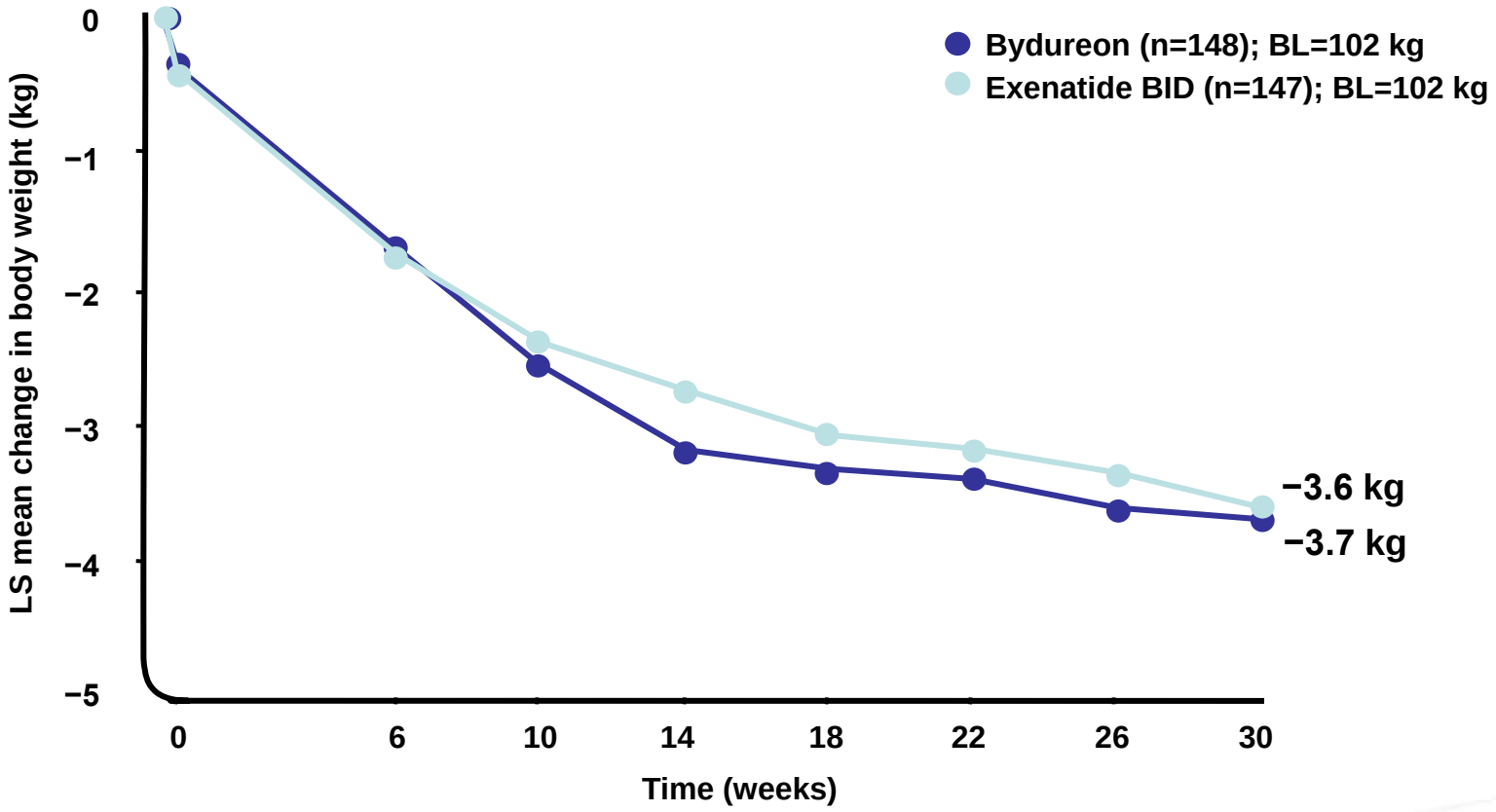
DURATION-1: continuous exenatide exposure – HbA_{1C} reduction due to significant reductions in both FPG and PPG



***P*<0.05.**

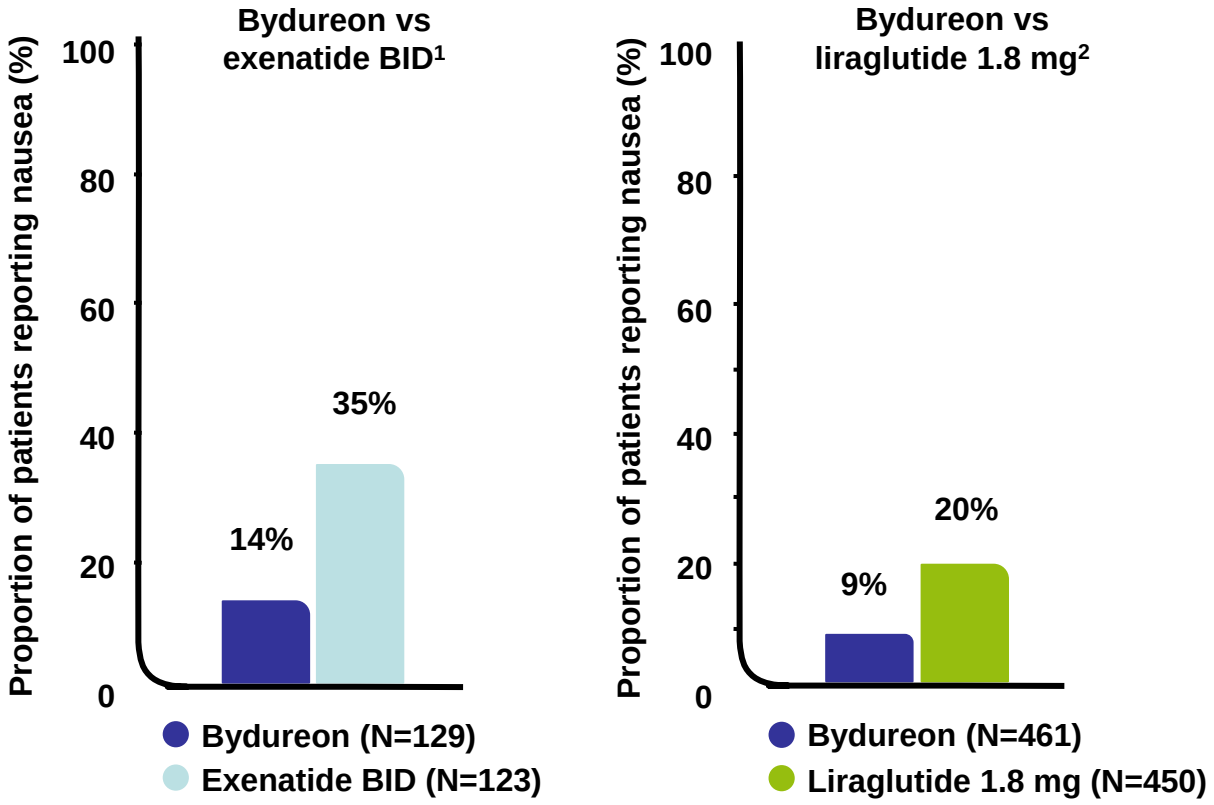
Drucker DJ, *et al*. *Lancet*. 2008;372:1240-1250

DURATION-1: weight loss* similar to exenatide BID†



*Bydureon is not indicated for the management of obesity, and weight change was a secondary endpoint in clinical trials.
†ITT population.
Drucker DJ, et al. *Lancet*. 2008;372:1240-1250.

Bydureon demonstrated lower incidence of nausea than exenatide BID and liraglutide 1.8 mg



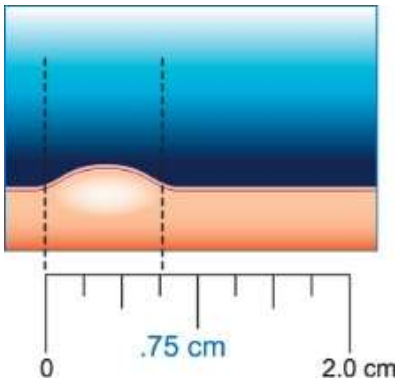
Percentage of patients reporting at least one episode of nausea was lower with Bydureon than with exenatide BID[1] and with liraglutide 1.8 mg[2]

1. Blevins T, et al. *J Clin Endocrin Metab*. 2011;96:1301-1310; 2. Buse J, et al. *Lancet.* 2013;381(9861):117-124.

Injection site considerations (cont'd)

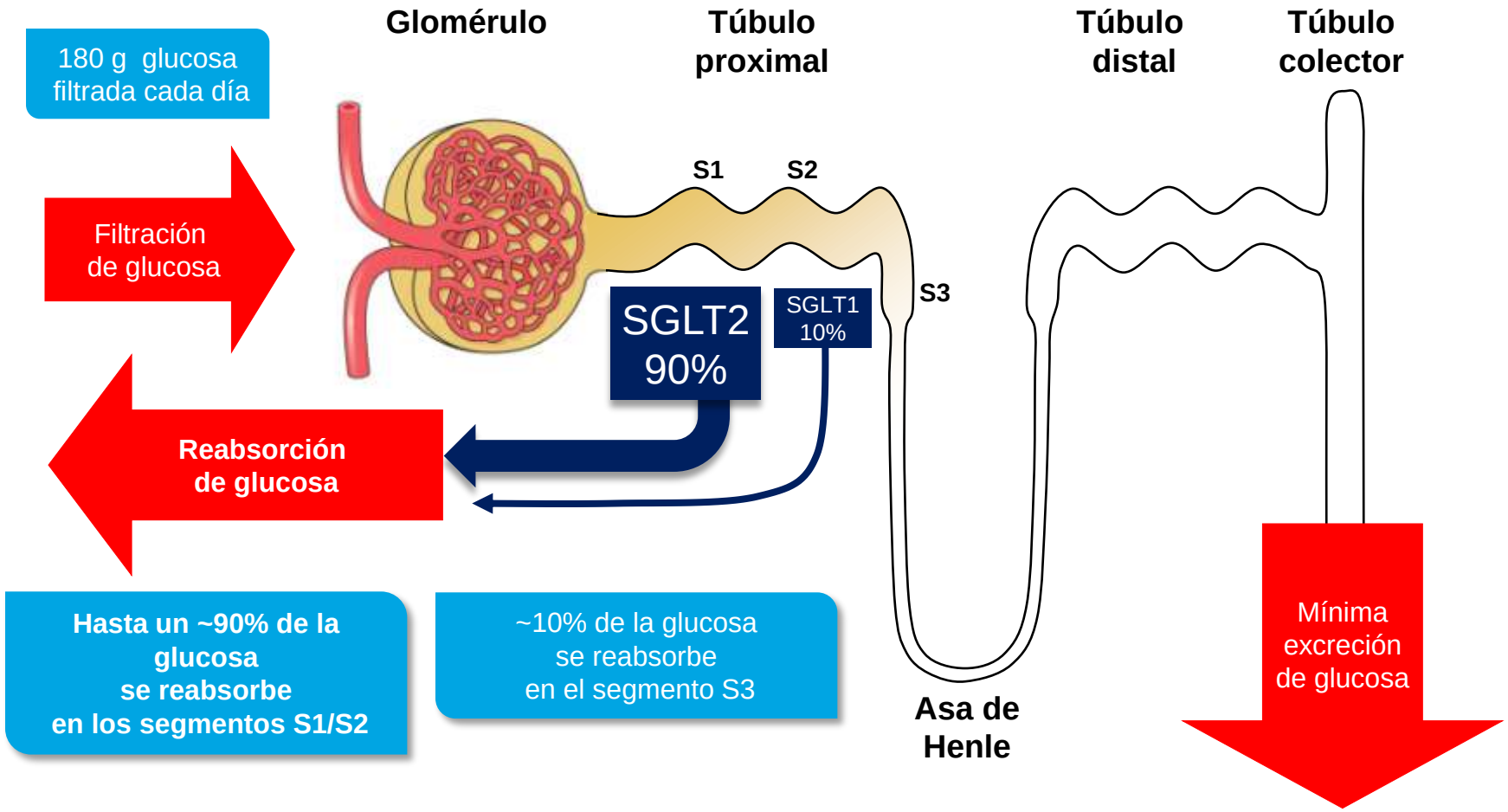
Injection site nodules

- Small subcutaneous injection site nodules were observed frequently, consistent with the known properties of Medisorb® microsphere formulations[1]
- These small bumps, which may not be detected visually, ranged in size from <0.25 cm to >2.0 cm, were asymptomatic, and resolved over 4 to 8 weeks[1,2]



Patients may notice small, raised bump that is about the size of a pea

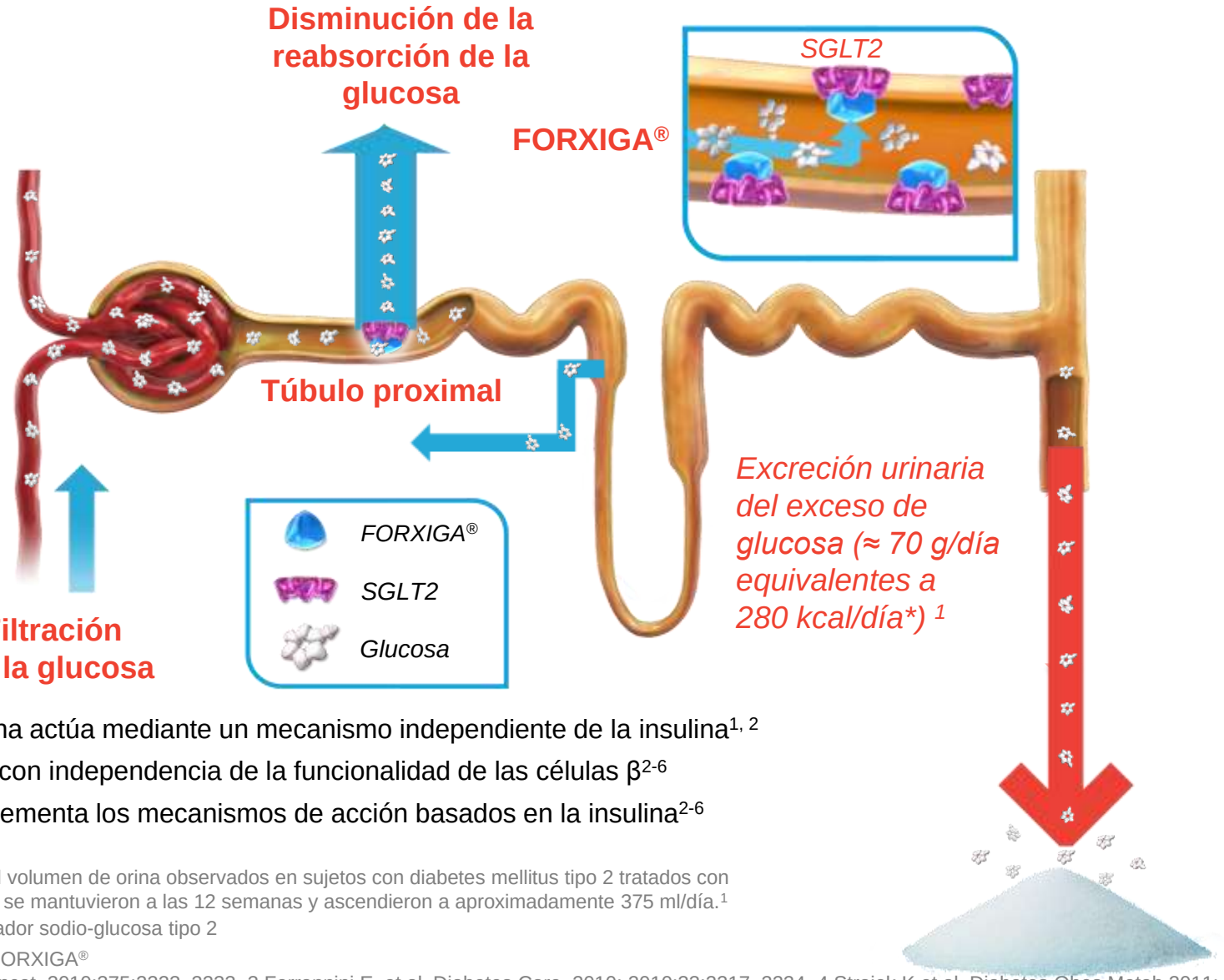
El 90% de la glucosa se reabsorbe en el túbulo proximal mediante los cotransportadores SGLT2



SGLT1: Cotransportador sodio-glucosa tipo 1; SGLT2: Cotransportador sodio-glucosa tipo 2

Adaptado de Bailey CJ. Trends in Pharmacological Sciences 2011;32 (2):63-71

FORXIGA® (dapagliflozina) reduce la reabsorción renal de glucosa y produce su excreción por la orina[1]



Dapagliflozina actúa mediante un mecanismo independiente de la insulina[1, 2]

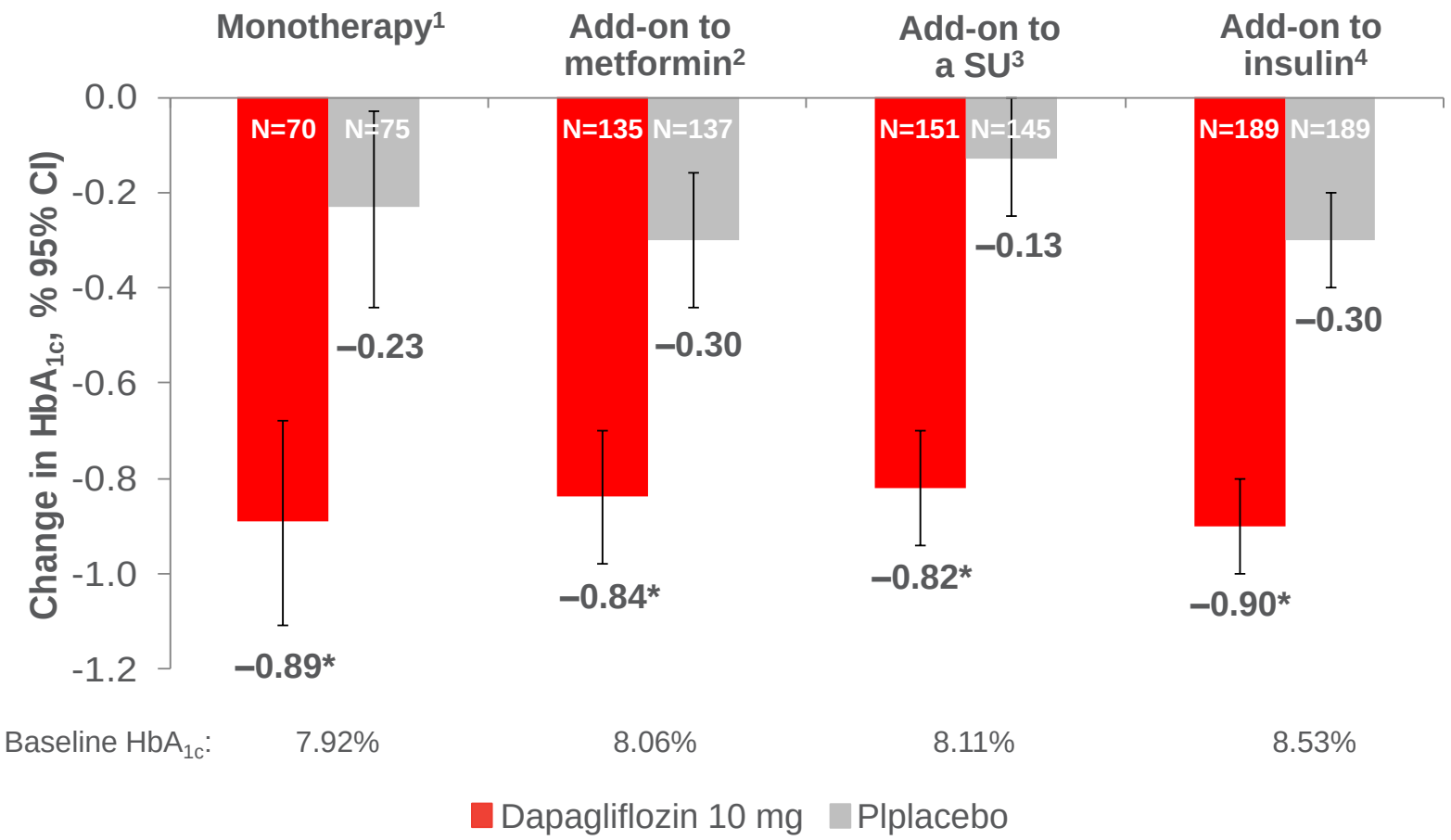
- Actúa con independencia de la funcionalidad de las células β[2-6]
- Complementa los mecanismos de acción basados en la insulina[2-6]

*Los incrementos del volumen de orina observados en sujetos con diabetes mellitus tipo 2 tratados con dapagliflozina 10 mg se mantuvieron a las 12 semanas y ascendieron a aproximadamente 375 ml/día.[1]

SGLT2: Cotransportador sodio-glucosa tipo 2

1. Ficha técnica de FORXIGA®
2.Bailey CJ, et al. Lancet. 2010;375:2223–2233. 3.Ferrannini E, et al. Diabetes Care. 2010; 2010;33:2217–2224. 4.Strojek K et al. Diabetes Obes Metab 2011; 13:928-938. 5. Nauck MA, et al. Diabetes Care 2011;34:2015–22; 2. 6.Wilding J.P.H et al Ann Intern Med. 2012;156:405-415.

Consistent reduction in HbA_{1c} at Week 24 across studies



The above are not head to head studies and direct comparisons should not be made.
*Statistically significant versus placebo using Dunnett's correction; adjusted mean change from baseline using ANCOVA, excluding data after rescue (LOCF).

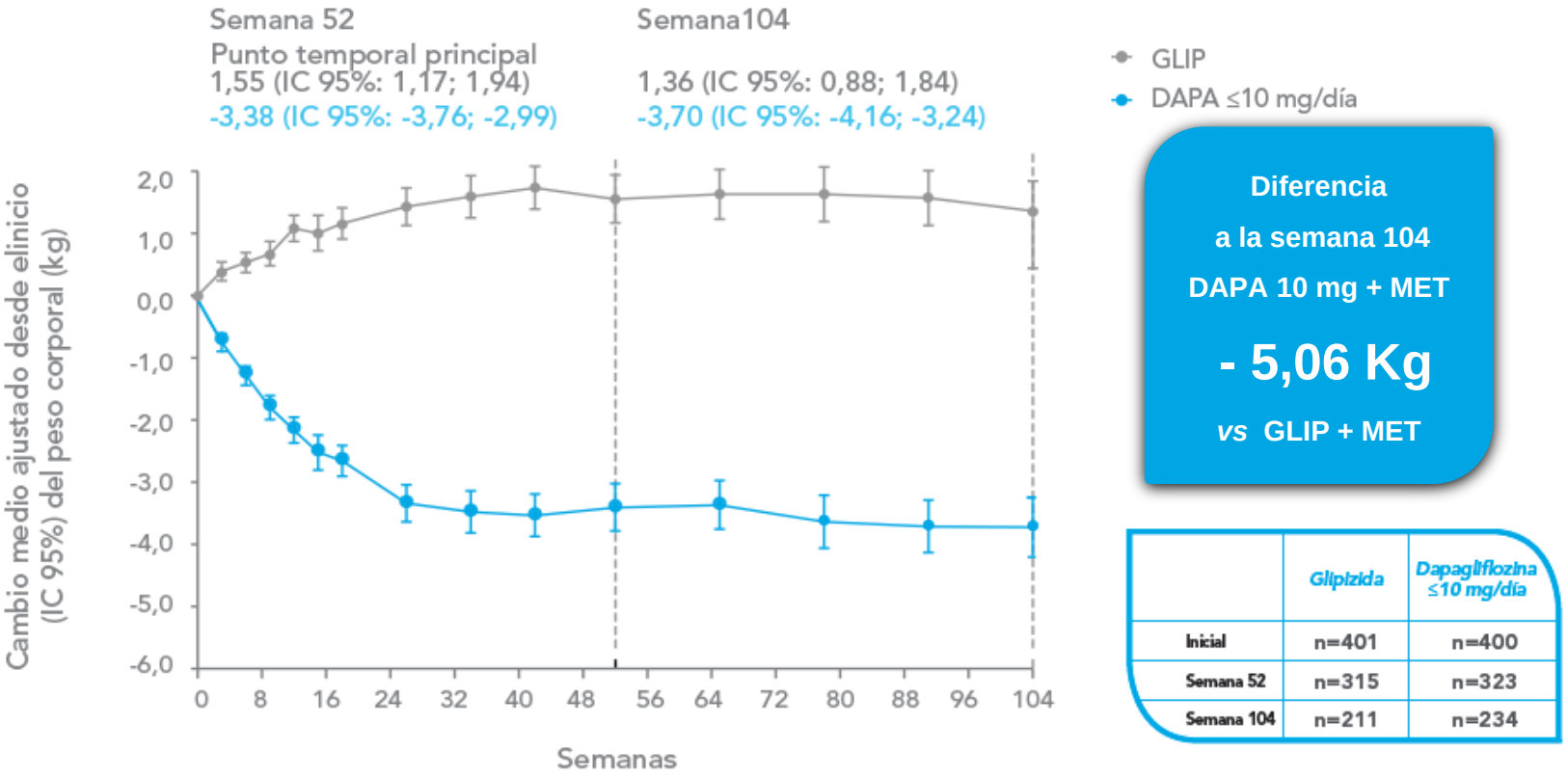
ANCOVA, analysis of covariance; LOCF, last observation carried forward.

1. Ferrannini E, *et al. Diabetes Care* 2010;**33**:2217–24; 2. Bailey CJ, *et al. Lancet* 2010;**375**:2223–33; 3. Strojek K, *et al. Diabetes Obes Metab* 2011;**13**:928–38; 4. Wilding J, *et al*. *Diabetes* 2010;**59**(Suppl 1):0078-OR.

FORXIGA® (dapagliflozina) produce una pérdida de peso significativa y sostenida en el tiempo[1,2]

- Variaciones en el peso corporal a las 52 semanas:[1*]
  - FORXIGA® + metformina: -3,2 kg; p<0,0001
  - Glipizida + metformina: +1,2 kg

- FORXIGA® 10 mg presenta una disminución sostenida del peso corporal (104 semanas)[2]



Diferencia
a la semana 104
DAPA 10 mg + MET

- 5,06 Kg

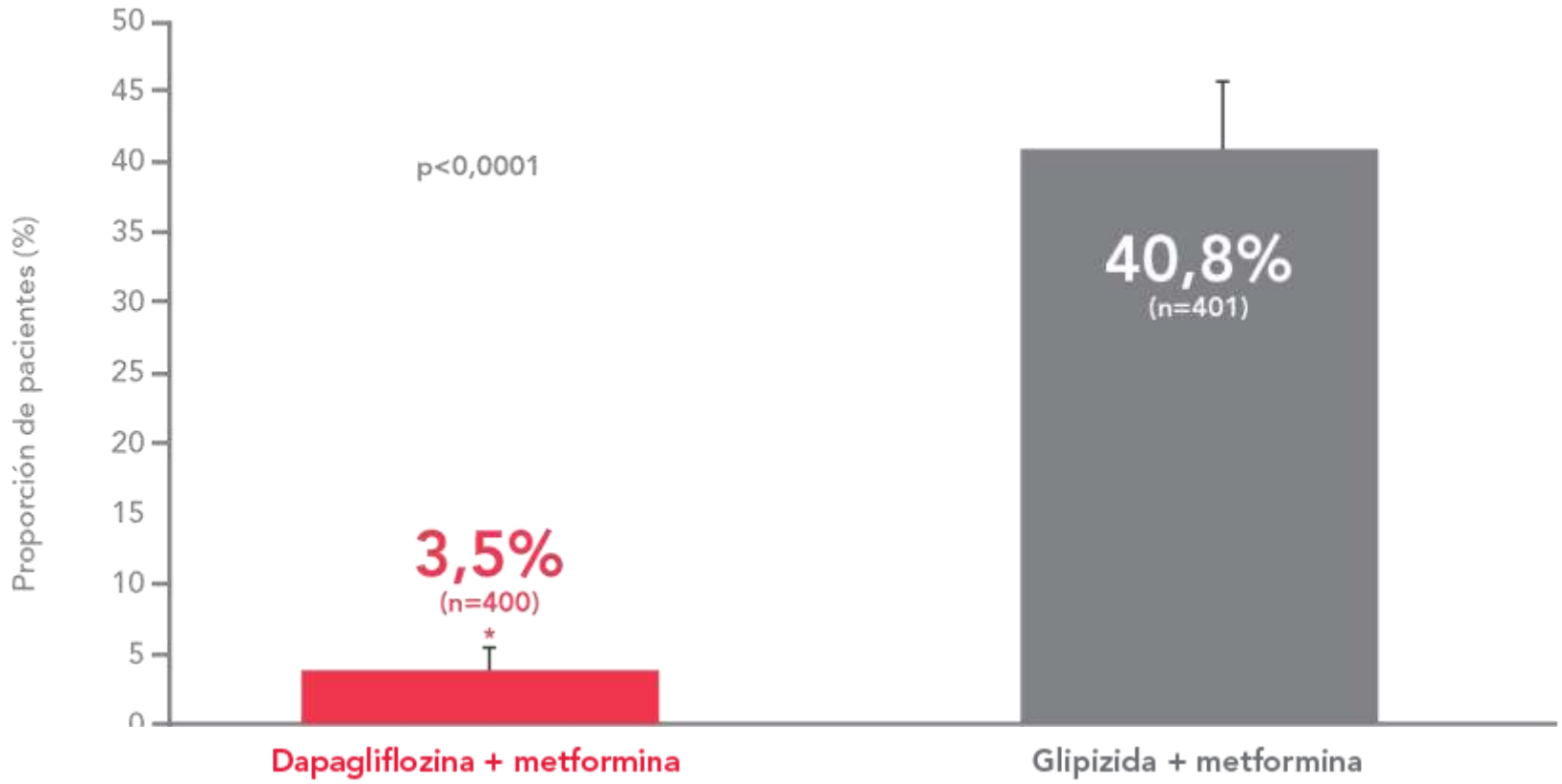
***vs* GLIP + MET**

	Glipizida	*Dapagliflozina ≤10 mg/día*
Inicial	n=401	n=400
Semana 52	n=315	n=323
Semana 104	n=211	n=234

* Los datos corresponden a un cambio medio ajustado respecto al momento inicial con un IC de 95% derivados de ANCOVA utilizando los valores de LOCF
DAPA: Dapagliflozina; MET: Metformina; GLI: Glipizida ; IC: Intervalo de confianza LOCF: Última observación disponible; ANCOVA: Análisis de covarianza

1. Nauck MA, et al. Diabetes Care 2011;34:2015–22 2. Bailey CJ, Wilding, JPH, Nauck M, et al. Sustained Reductions in Weight and HbA1c with Dapagliflozin: Long-term Results from Phase III Clinical Studies in Type 2 Diabetes. Poster 721 presentado en 48th EASD Meeting, 1–5 octubre 2012; Berlin, Germany.

FORXIGA® (dapagliflozina) disminuye en más de 10 veces los episodios de hipoglucemia en comparación con una SU



Pacientes con ≥1 episodio hipoglucémico a 1 año (criterio de valoración secundario)

*Diferencia vs. GLIP + MET, -37,2% (IC 95% de la diferencia -42,3 a -21,2; p< 0,0001)

SU: Sulfonilurea; GLIP: Glipizida; MET: Metformina

Nauck MA, et al. Diabetes Care 2011;34:2015–22

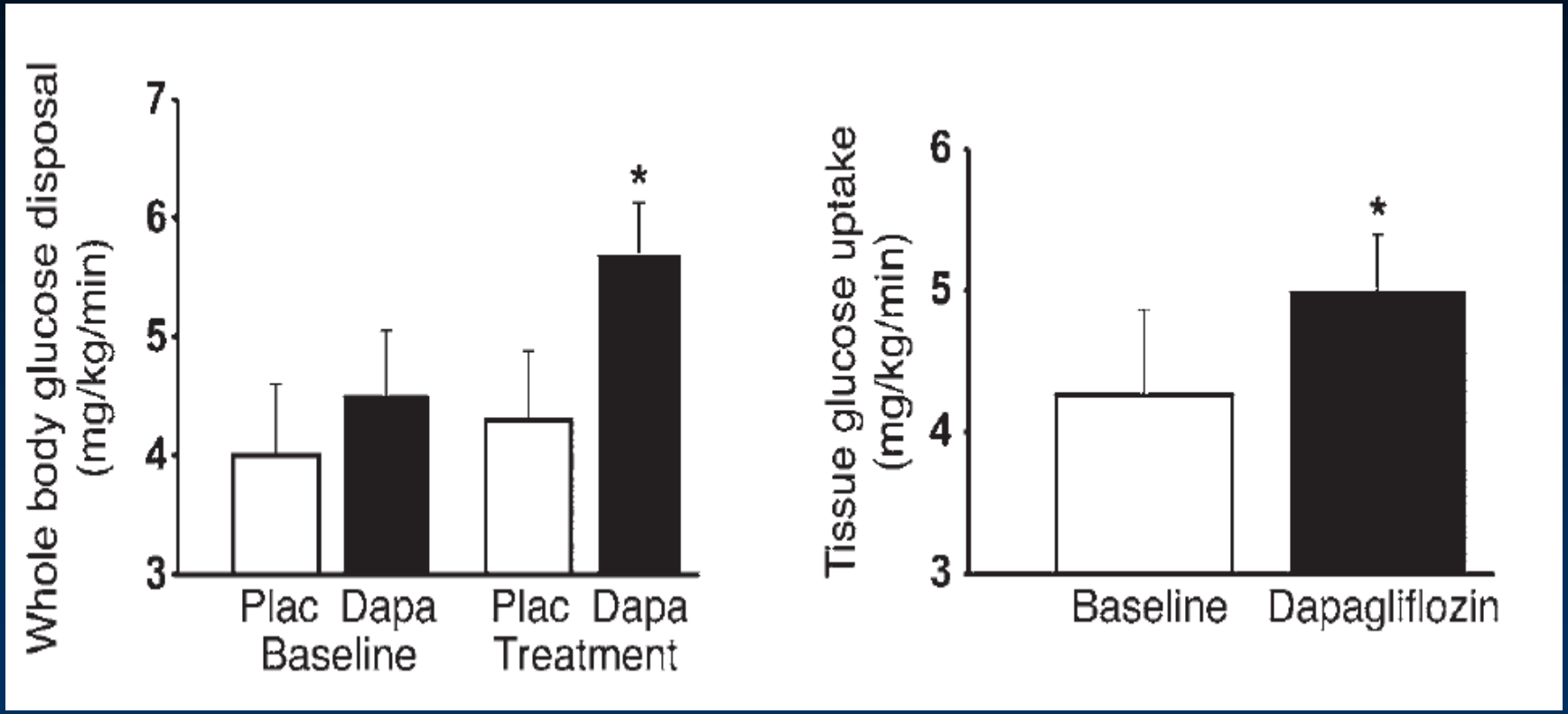
Dapagliflozin improves muscle insulin sensitivity but enhances endogenous glucose production

Aurora Merovci, Carolina Solis-Herrera, Giuseppe Daniele, Roy Eldor, Teresa Vanessa Fiorentino, Devjit Tripathy, Juan Xiong, Zandra Perez, Luke Norton, Muhammad A. Abdul-Ghani, and Ralph A. DeFronzo

Diabetes Division, University of Texas Health Science Center, San Antonio, Texas, USA.

J Clin Invest 2014 (press)

Depiction of the elements of decision making used to determine appropriate efforts to achieve glycemic targets.



J Clin Invest 2014 (press)

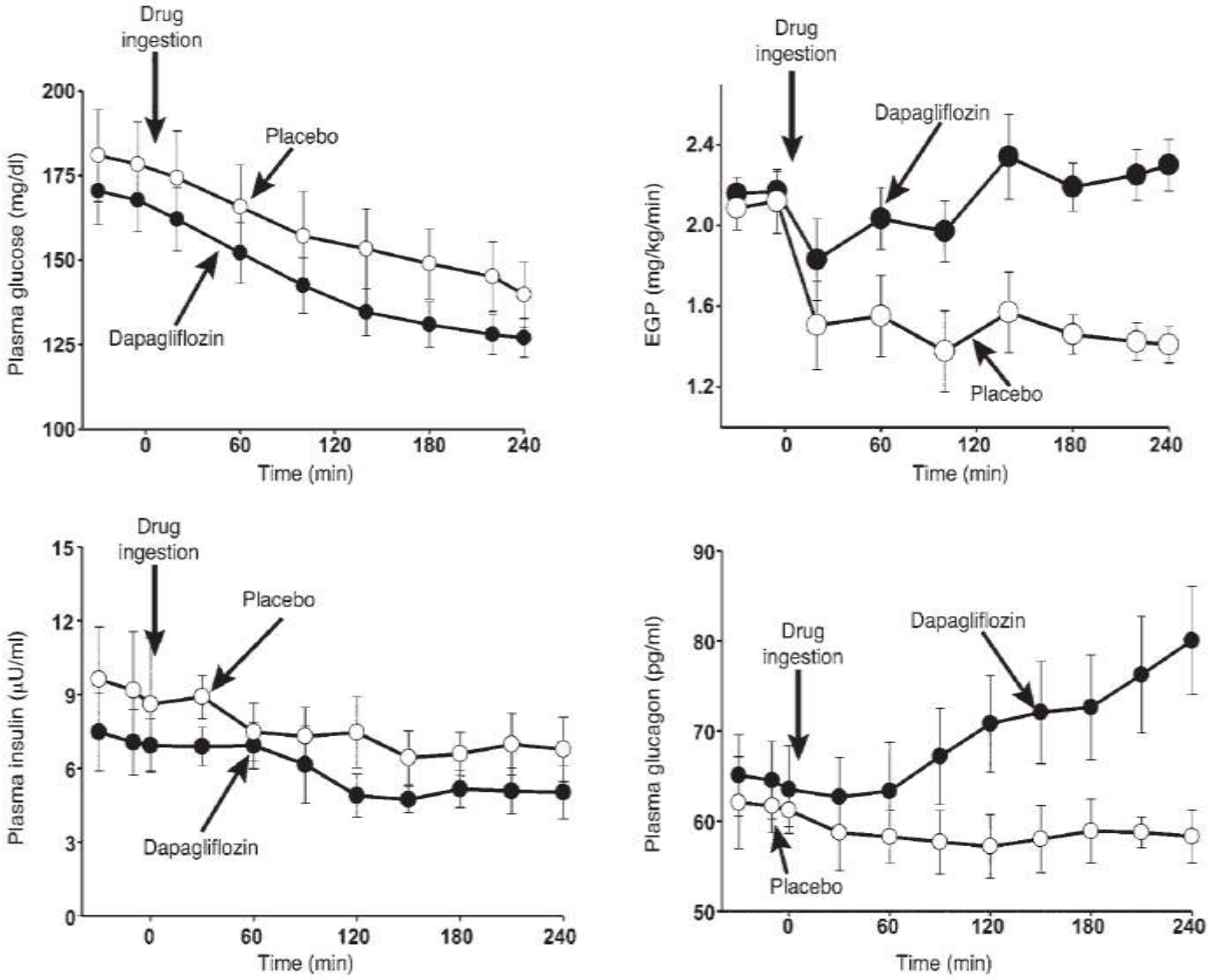


Figure 3

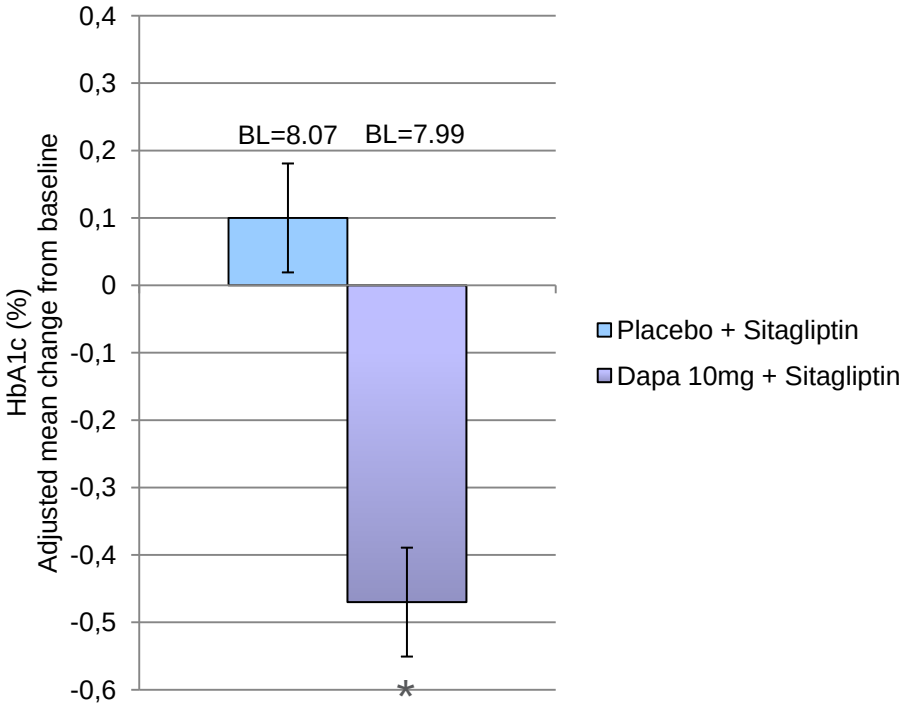
Plasma glucose, insulin, and glucagon concentrations and EGP in the study. On day 2, the ^{3}H-glucose infusion was started 3 hours before drug ingestion (time 0) and continued for 4 hours after drug ingestion (see Methods for more details).

J Clin Invest 2014 (press)

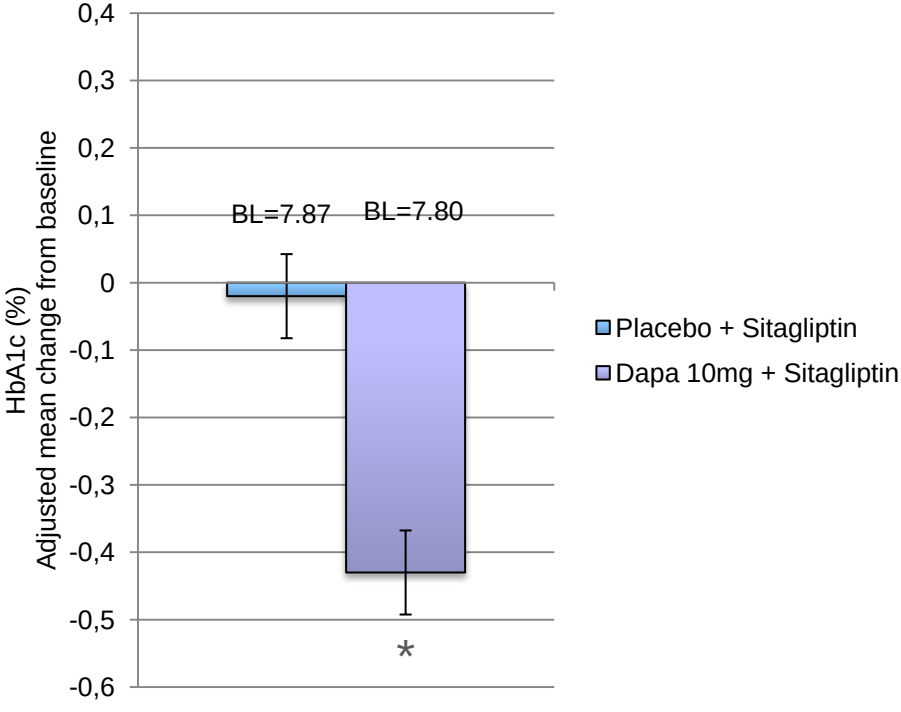
HbA1c (%) at Week 24 by Strata: Adjusted Mean Change from Baseline

FAS: excludes data after rescue

Add-on to sitagliptin monotherapy



Add-on to sitagliptin + metformin



* $p < 0.0001$

Jabbour et al Diabetes Care 2014; 37: 740-50

CONCLUSIONS

1- Flexibilitat: objectius, opcions terapèutiques

2- Postprandial: teràpia incretínica vs insulina ràpida

3- Setmanal: exenatide LAR

4- Quelcom nou: inhibidors SGLT-2: per continuar…

Generalitat de Catalunya
Departament de Salut

Bellvitge Hospital

Institut Català de la Salut