



Associazione Medici
Endocrinologi

Primo Congresso Interregionale AME Sud - Italia

Primo Congresso Interregionale ANIED Sud - Italia

Responsabile Scientifico Vincenzo Triggiani



Matera, 9-10 Maggio 2014 - HILTON GARDEN INN

La Terapia del Diabete: vecchie certezze

Achiropita Pucci

Endocrinologia ASP Cosenza

La Terapia del Diabete: dagli anni '90 ad oggi

Farmaco

Tolbutamide (Orinase)

Tolazamide* (Tolinase)

Acetoesamide* (Dymelor)¹

Clorpropamide* (Diabinese)¹

Gliburide
(Duabeta, Micronase)
(Glynase)

Glipizide*
(Glucotrol)
(Glucotrol XL)

Glimepiride (Amaryl)

Metformina (Glucophage)

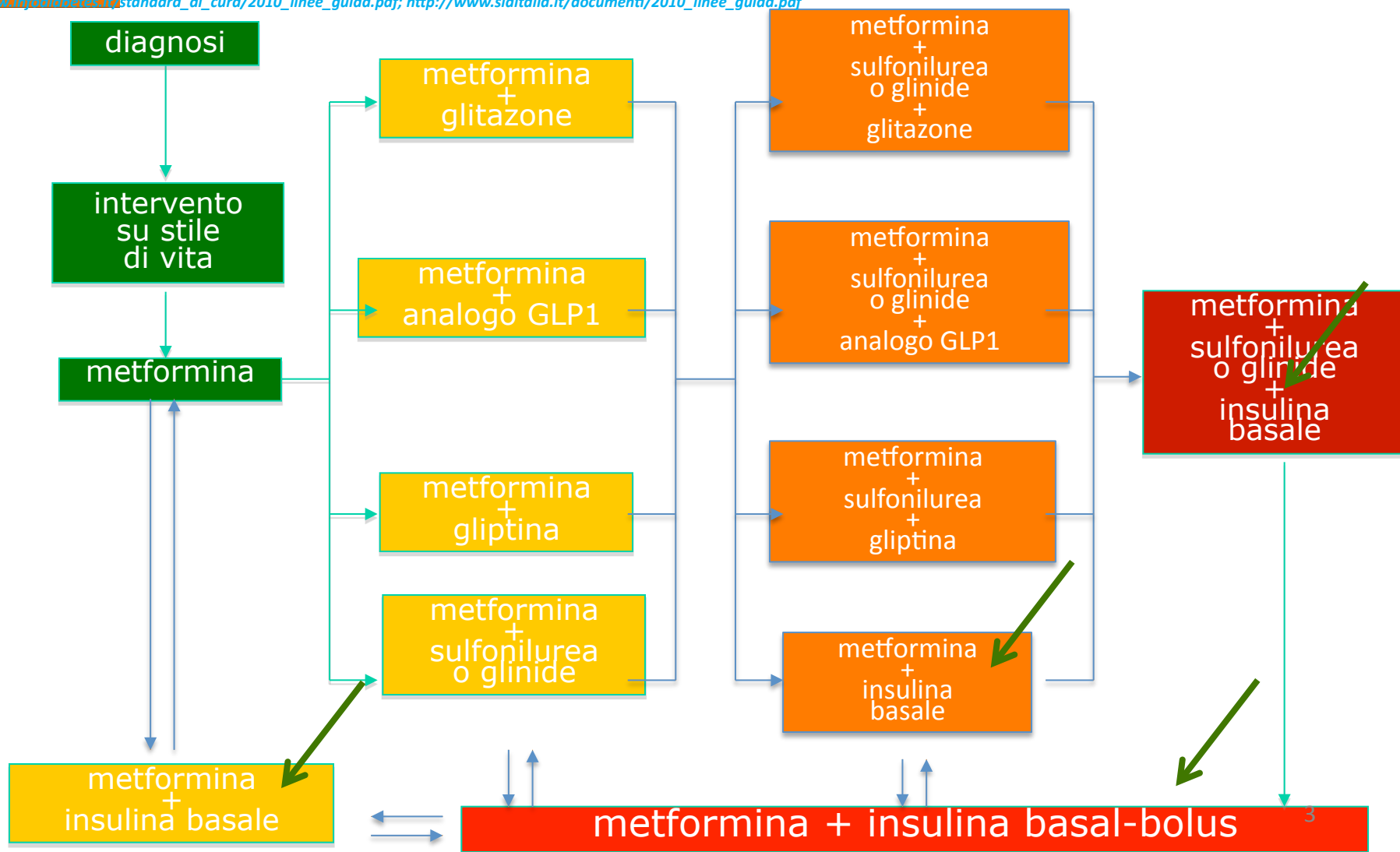
Acarbose (Precose)

Tabella 18-12. Sommario delle

	Tipo di insulina
Ad azione breve	Insulina lispro Regolare, Velosulin
Ad azione intermedia	Lenta, NPH
A lunga azione	Ultralenta

Flow-chart per la terapia del diabete mellito di tipo 2.

AMD, SID Standard italiani per la cura del diabete mellito 2009-2010
http://www.infodiabetes.it/standard_di_cura/2010_linee_guida.pdf; http://www.siditalia.it/documenti/2010_linee_guida.pdf

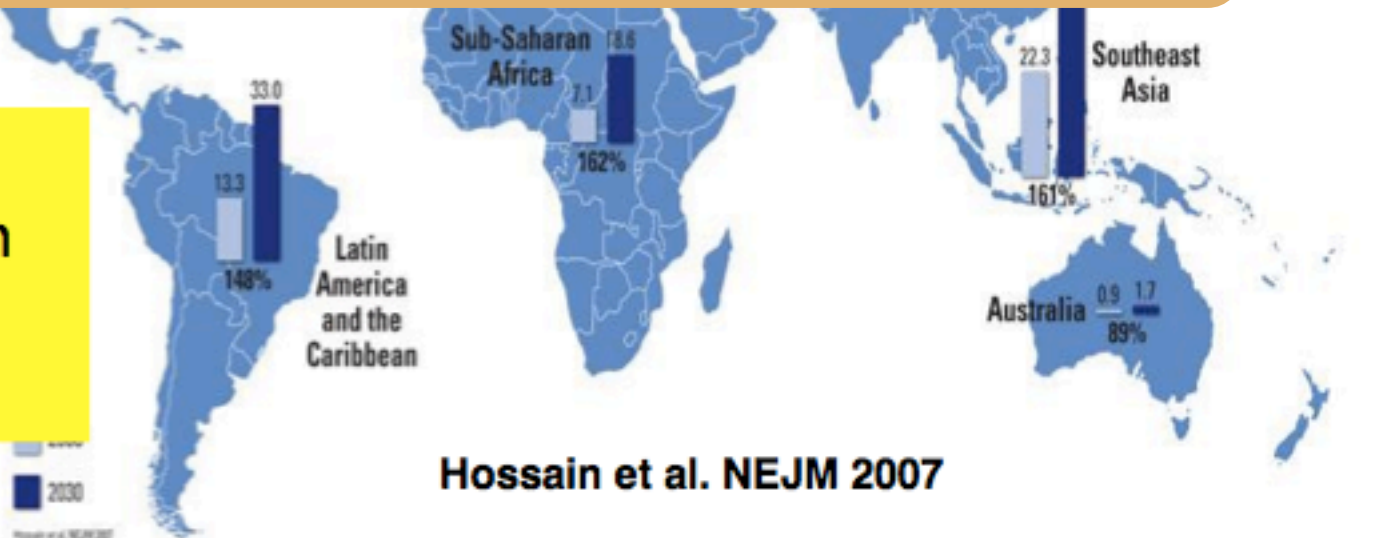


Prevalence of Diabetes 2030

Il Diabete di tipo 2 (DM2) è una malattia cronica evolutiva

La glicemia peggiora “progressivamente” nel tempo

2010
371 million
people
worldwide



Compenso glicemico e complicanze del diabete

Studio UKPDS

*memoria
metabolica*

- La diagnosi deve essere precoce, prima si avvia il trattamento migliori sono i risultati nel tempo
- Più bassa è la glicemia che si riesce a raggiungere all'inizio della terapia migliore sarà l'HbA1c nel tempo

Qualsiasi

Morti legate

Ogni causa di morte

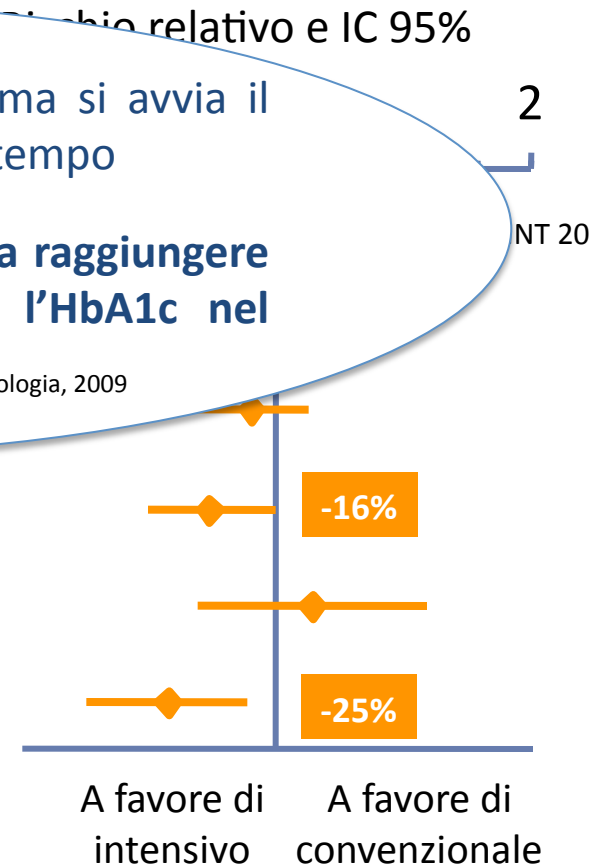
Infarto miocardico

Ictus

Microvascolari

Diabetes Care, 2009 – Diabetologia, 2009

0.84	0.052
1.11	0.52
0.75	0.0099



UKPDS 33, Lancet 1998;352 :837- 853

Recent Clinical Trials in High Risk CVD DM: Tight Glycemic Control and Macrovascular complications

Clinical Trials	ACCORD	ADVANCE	VADT
Total CVDs (1 st outcome)	10% reduction (NS)	6% reduction (NS)	13% reduction (NS)

non sembrano documentare alcun beneficio di un controllo glicemico intensivo sul rischio cardiovascolare

Nonfatal MI	24% reduction HR0.76(0.62-0.92)	2% reduction (NS)	3.2% reduction (NS)
Nonfatal stroke	6% increment (NS)	2% increment (NS)	35% reduction (NS)
Severe Hypoglycemia	3.1 % vs 1.0 % per year	0.7 % vs 0.4 % per year	3.5 % vs 1.6 % per year

Obiettivi terapia ipoglicemizzante

- Compenso glicometabolico
- Prevenzione complicanze cardiovascolari
- Evitare ipoglicemia
- Assicurare compliance paziente
- Assicurare qualità di vita

IDEALE

Agire sui meccanismi patogenetici della malattia diabetica

Non aumentare il peso corporeo

Risparmiare" la Beta-cellula

Durability

Avere un basso costo

Obiettivi terapia ipoglicemizzante

- **Compenso glicometabolico**
- Prevenzione complicanze cardiovascolari
- Evitare ipoglicemia
- Assicurare compliance paziente
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IDEALE

Agire sui meccanismi patogenetici della malattia diabetica

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Compenso glicometabolico

Obiettivi glicemici in diabetici adulti di tipo 1 e 2

HbA_{1c} < 7,0%* (< 6,5% in singoli pazienti)

Glicemia a digiuno e pre-prandiale 70-130 mg/dl

Glicemia post-prandiale[§] < 180 mg/dl^{§#}

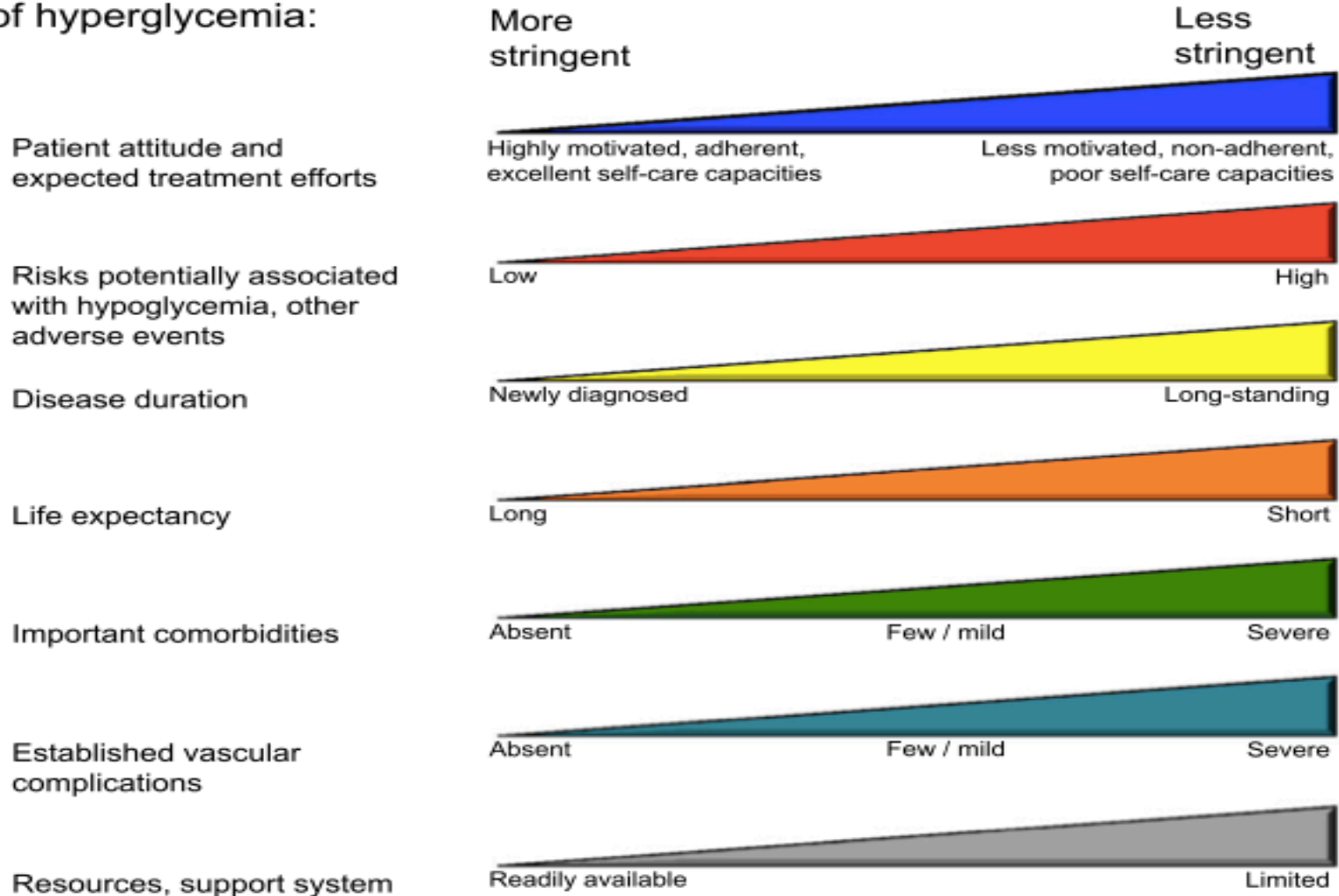
*Facendo riferimento ai valori di 4,0-6,0% della popolazione non diabetica, con il metodo utilizzato dal DCCT.

[§]La misurazione della glicemia post-prandiale deve essere effettuata 2 ore dopo l'inizio del pasto.

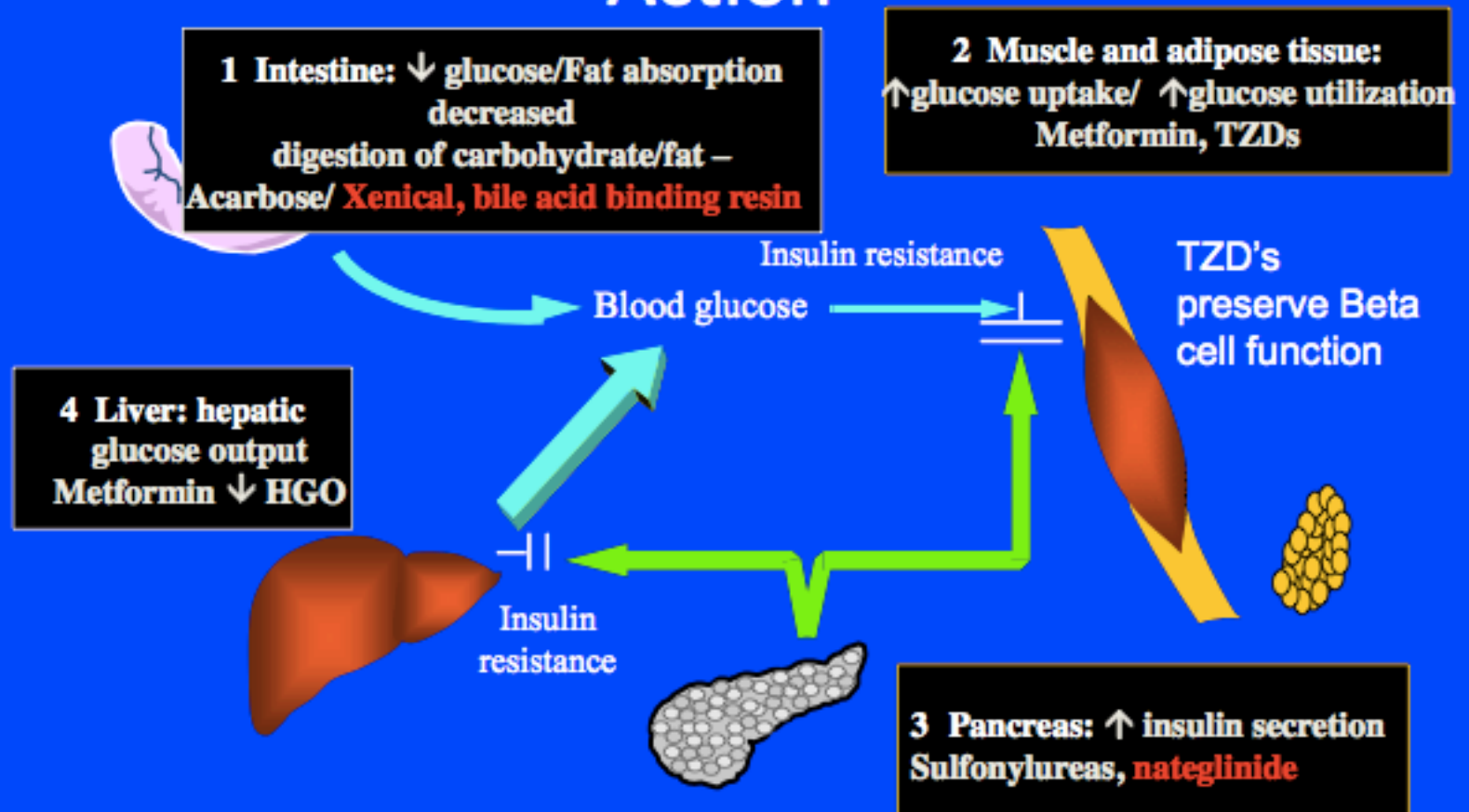
[#]Valori post-prandiali < 140 mg/dl sono perseguibili nel diabete tipo 2 (IDF 2007).

Consensus ADA EASD

Approach to management of hyperglycemia:



Azione fisiopatogenetica farmaci



DeFronzo RA. *Diabetes*. 1988;37:667-687. Lebovitz HE. In *Joslin's Diabetes Mellitus*. 1994:508-529;
Amatruda JM. In: *Diabetes Mellitus*. 1996. DeFronzo RA et al. *J Clin Endocrinol Metab*. 1991;73:1294-1301.
Whitcomb RW et al. In: *Diabetes Mellitus*. 1996; Cavaghan MK et al. *J Clin Invest*. 1997;100:530-537.
Ehrmann DA et al. *J Clin Endocrinol Metab*. 1997;82:2108-2116; Wolffenbuttel BHR. *Eur J Clin Pharmacol*. 1993;45:113-116

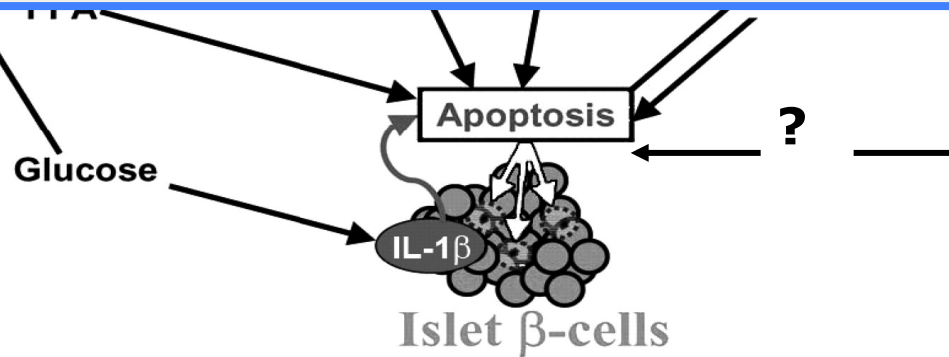
Danno β -cellulare e patogenesi del diabete tipo 2



Diabetes Metab. 2008 Feb;34 Suppl 2:S56-64. doi: 10.1016/S1262-3636(08)73396-2.

Beta-cell apoptosis in type 2 diabetes: quantitative and functional consequences.

[Lupi R1, Del Prato S.](#)



Healthy eating, weight control, increased physical activity

Metformin

high
low risk
neutral/loss
GI / lactic acidosis
low

If needed to reach individualized HbA_{1c} target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference):

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea ^b	Thiazolidinedione	DPP-4 Inhibitor	GLP-1 receptor agonist	Insulin (usually basal)
high moderate risk gain hypoglycemia ^c low	high low risk gain edema, HF, Fx ^s ^c	intermediate low risk neutral rare ^c	high low risk loss GI ^c	highest high risk gain hypoglycemia ^c variable

L'aggiunta di farmaci è la regola e non l'eccezione

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea ^b	Thiazolidinedione	DPP-4 Inhibitor	GLP-1 receptor agonist	Insulin (usually basal)
+ TZD or DPP-4-i or GLP-1-RA or Insulin ^d	+ SU ^b or DPP-4-i or GLP-1-RA or Insulin ^d	+ SU ^b or TZD or Insulin ^d	+ SU ^b or TZD or Insulin ^d	+ TZD or DPP-4-i or GLP-1-RA

If combination therapy that includes basal insulin has failed to achieve HbA_{1c} target after 3-6 months, proceed to a more complex insulin strategy, usually in combination with one or two non-insulin agents:

**Insulin^e
(multiple daily doses)**

Intervento su stile di vita

Am J Clin Nutr. 2004 Aug;80(2):257-63.

Weight management through lifestyle modification for the prevention and management of type 2 diabetes: rationale and strategies. A statement of the American Diabetes Association, the North American Association for the Study of Obesity, and the American Society for Clinical Nutrition.

[Klein S¹, Sheard NF, Pi-Sunyer X, Daly A, Wylie-Rosett J, Kulkarni K, Clark NG; American Diabetes Association; North American Association for the Study of Obesity; American Society for Clinical Nutrition.](#)

J Am Coll Nutr. 2003 Oct;22(5):331-9.

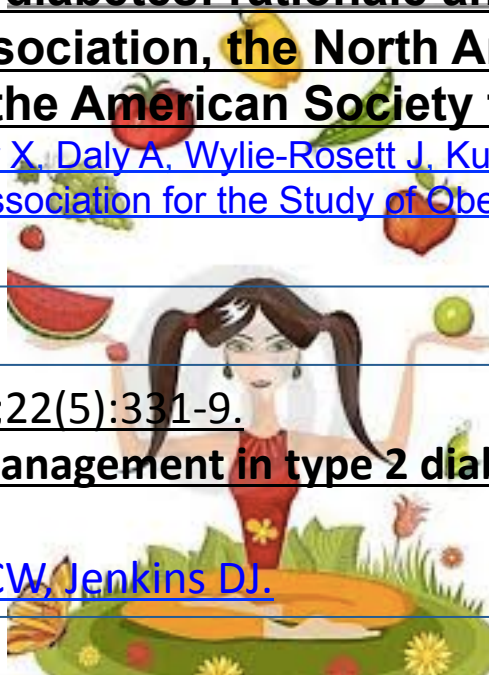
Importance of weight management in type 2 diabetes: review with meta-analysis of clinical studies.

[Anderson JW¹, Kendall CW, Jenkins DJ.](#)

BMJ. 2010 Jul 20;341:c3337. doi: 10.1136/bmj.c3337.

Nutritional intervention in patients with type 2 diabetes who are hyperglycaemic despite optimised drug treatment--Lifestyle Over and Above Drugs in Diabetes (LOADD) study: randomised controlled trial.

[Coppell KJ¹, Kataoka M, Williams SM, Chisholm AW, Vorgers SM, Mann JJ.](#)



Agenti anti-iperglicemici per il diabete di tipo 2

Classe	Riduzione dell'HbA1c	Ipoglicemia	Variazioni ponderali	Fattori di rischio CVD	Dosaggio (volte/die)	Controindicazioni per comorbidità
Metformina	1.5	No	Nessuna	Minimi	2	reni e fegato
Insulina a lento rilascio	1.5 – 2.5	Sì	Aumento	TG	1 iniezione	Nessuna
Insulina ad azione rapida	1.5 – 2.5	Sì	Aumento	TG	1-4 iniezioni	Nessuna
Sulfoniluree	1.5	Sì	Aumento	Nessuno	1	Essenzialmente nessuna
Tiazolidinedioni	0.5 – 1.4	No	Aumento	Variabili	1	CHF, fegato
Repaglinide	1 – 1.5	Sì	Aumento	Nessuno	3	Essenzialmente nessuna
Nateglinide	0.5 – 0.8	Raramente	Aumento	Nessuno	3	Essenzialmente nessuna
Inibitori dell'alfa-glucosidasi	0.5 – 0.8	No	Nessuna	Minimi	3	Essenzialmente nessuna
Analoghi dell'amilina	0.5 – 1.0	No	Riduzione	Con calo ponderale	3 iniezioni	Nessuna
Agonisti del GLP-1R	0.5 – 1.0	No	Riduzione	Con calo ponderale	2 iniezioni	Reni
Inibitori del DPP-4	0.6 – 0.8	No	Nessuna	Nessuno	1	Nessuna
Sequestranti degli acidi biliari	0.5	No	Nessuna	LDL	1-2	TG severa
Bromocriptina	0.7	No	Nessuna	Minimi	1	Essenzialmente

Metformina

Vantaggi

- Riduzione insulina

Lancet. 1998 Sep 12;352(9131):854-65.

Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group.

- Effetto favorevole su livelli Tg, LDL, HDL, PAI1, PCR
- Basso costo

Svantaggi

- Non sempre efficace in

- Acidosi lattica (0,05 casi/1000pz/anno)

Oral Pharmacologic Treatment of Type 2 Diabetes Mellitus: A Clinical Practice Guideline From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Linda L. Humphrey, MD, MPH; Donna E. Sweet, MD; Melissa Starkey, PhD; and Paul Shekelle, MD, PhD, for the Clinical Guidelines Committee of the American College of Physicians*

Comparison	HbA _{1c}	Weight/BMI	LDL Cholesterol	HDL Cholesterol	Triglycerides
Monotherapy vs. monotherapy					
Metformin vs.					
TZD	Neither favored, moderate	Favors metformin, high	Favors metformin, moderate† Favors metformin, high‡	Neither favored, moderate† Favors pioglitazone, high‡	Favors metformin, moderate† Favors pioglitazone, high‡
Sulfonylurea	Neither favored, high	Favors metformin, high	Favors metformin, high	Neither favored, high	Favors metformin, moderate
DPP-4 inhibitor	Favors metformin, moderate	Favors metformin, moderate	Favors metformin, moderate	Neither favored, low	Neither favored, low
Meglitinide	Neither favored, low§ Favors metformin,	Unclear, low	Unclear, low	Unclear, low	Unclear, low

Monotherapy vs. combination therapy

Metformin vs.

Metformin + TZD	Favors metformin + TZD, high	Favors metformin, high	Favors metformin, high† Unclear, low‡	Favors metformin + rosiglitazone, high† Favors metformin + pioglitazone, low‡	Favors metformin, high† Unclear, low‡
Metformin + sulfonylurea	Favors metformin + sulfonylurea, high	Favors metformin, high	Neither favored, low	Neither favored, low	Neither favored, low
Metformin + DPP-4 inhibitor	Favors metformin + DPP-4 inhibitor, moderate	Neither favored, moderate	Neither favored, low	Neither favored, moderate	Favors metformin + DPP-4 inhibitor, low
Metformin + meglitinide	Favors metformin + meglitinides, low	Favors metformin, low	Unclear, low	Neither favored, low	Favors metformin + meglitinides, low

Terapia insulinica

Vantaggi

- Azione fisiologica
- Maggior riduzione HbA1c
- Non richiede residua funzionalità β cellulare
- Possibile azione trofica β cell
- Non aumenta mortalità CHV

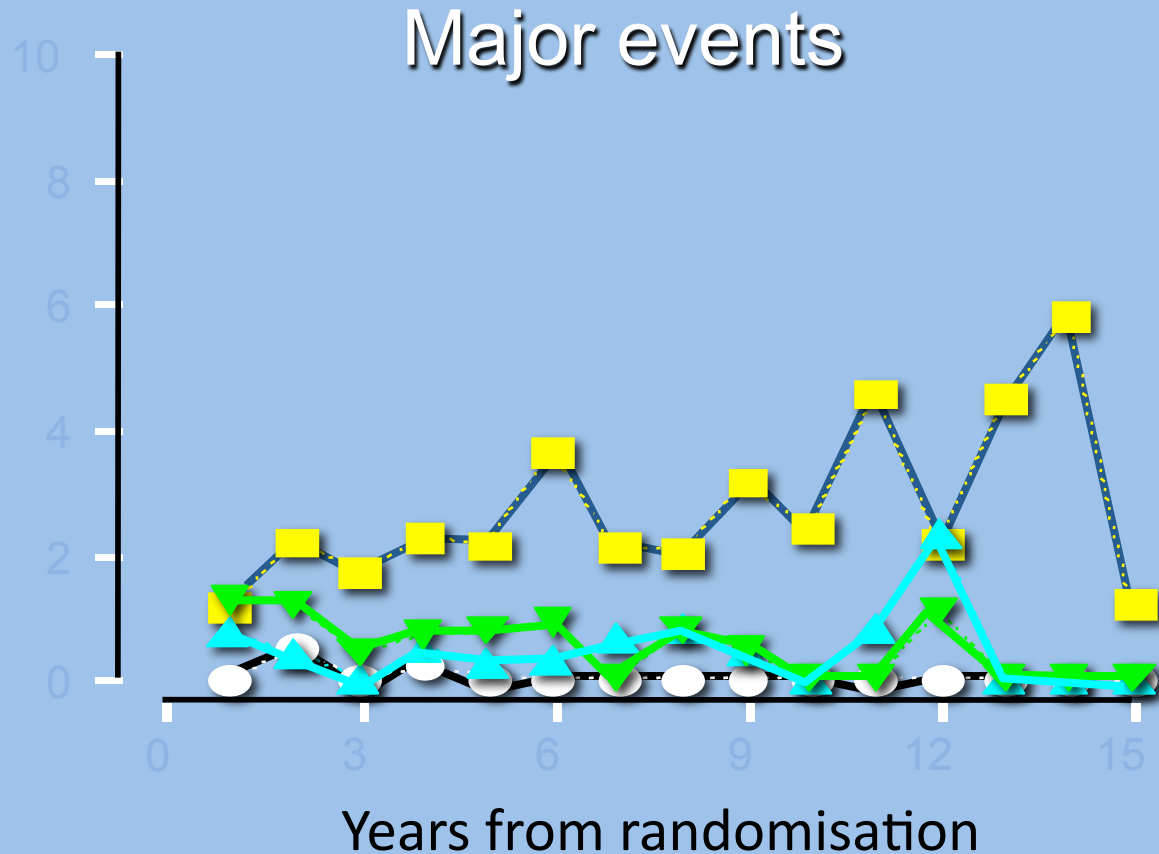
Svantaggi

- Ipoglicemie
- Compliance paziente

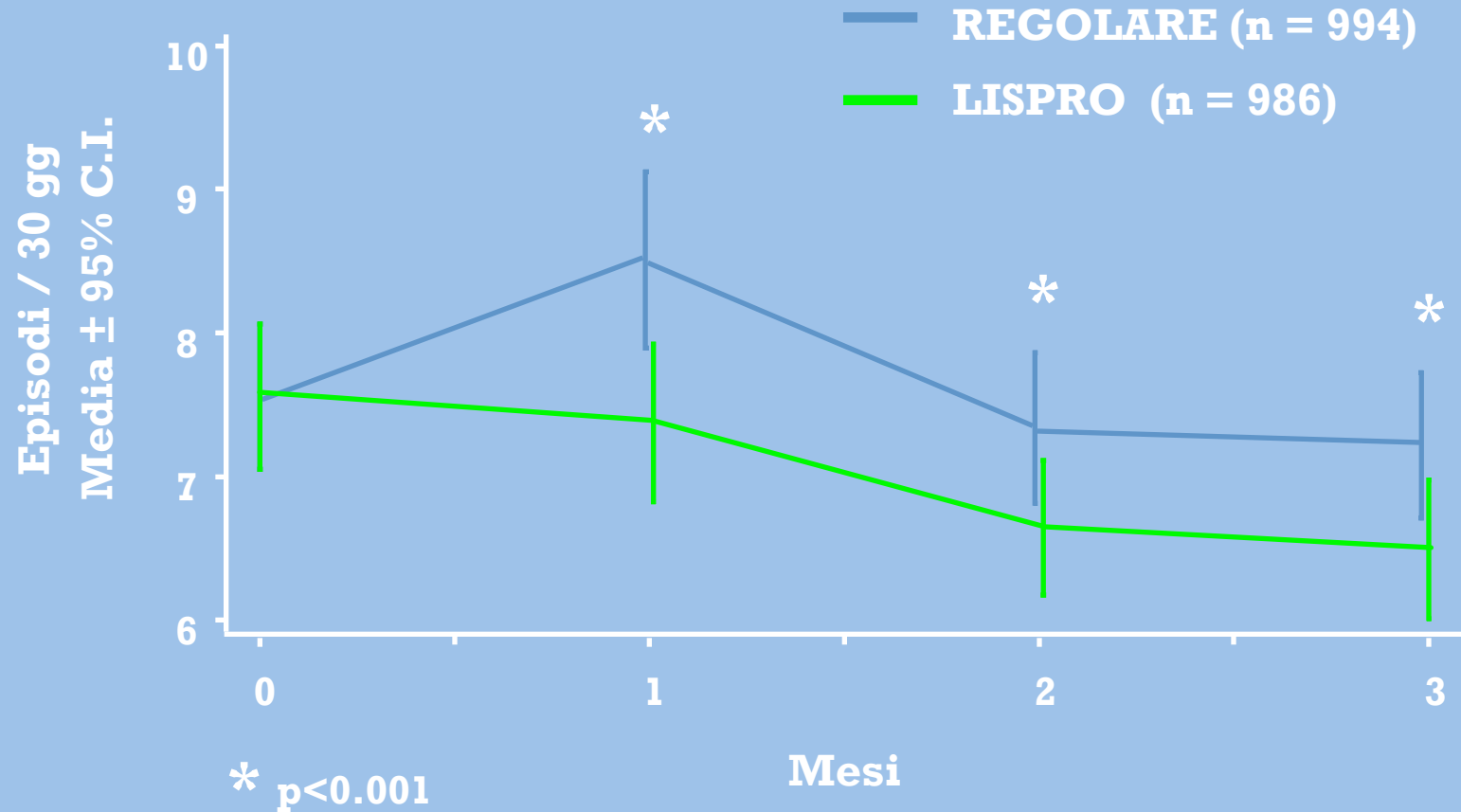
UKPDS:

Major hypoglycemic events per year

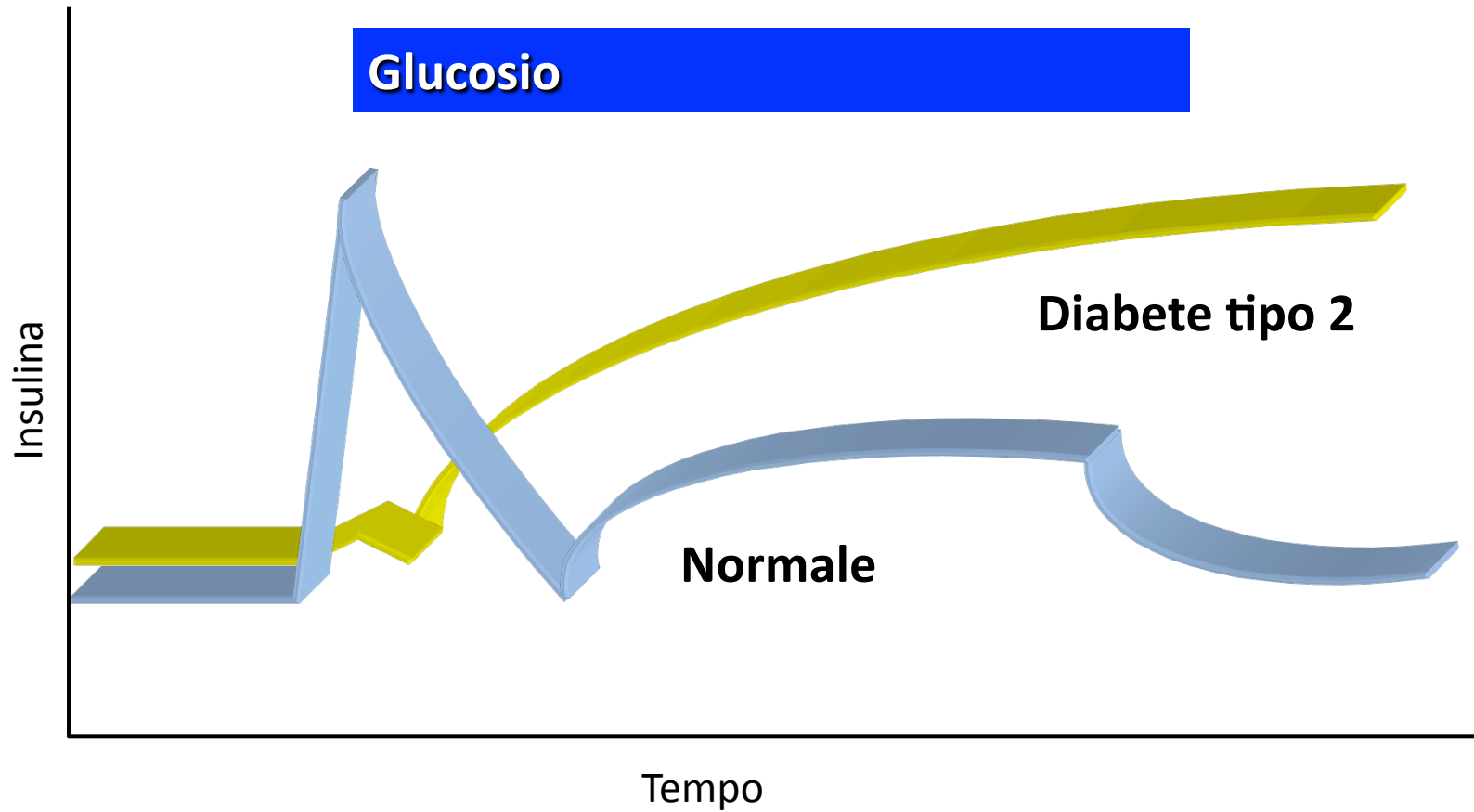
■ Insulin ▼ Glibenclamide ▲ Chlorpropamide ● Conventional



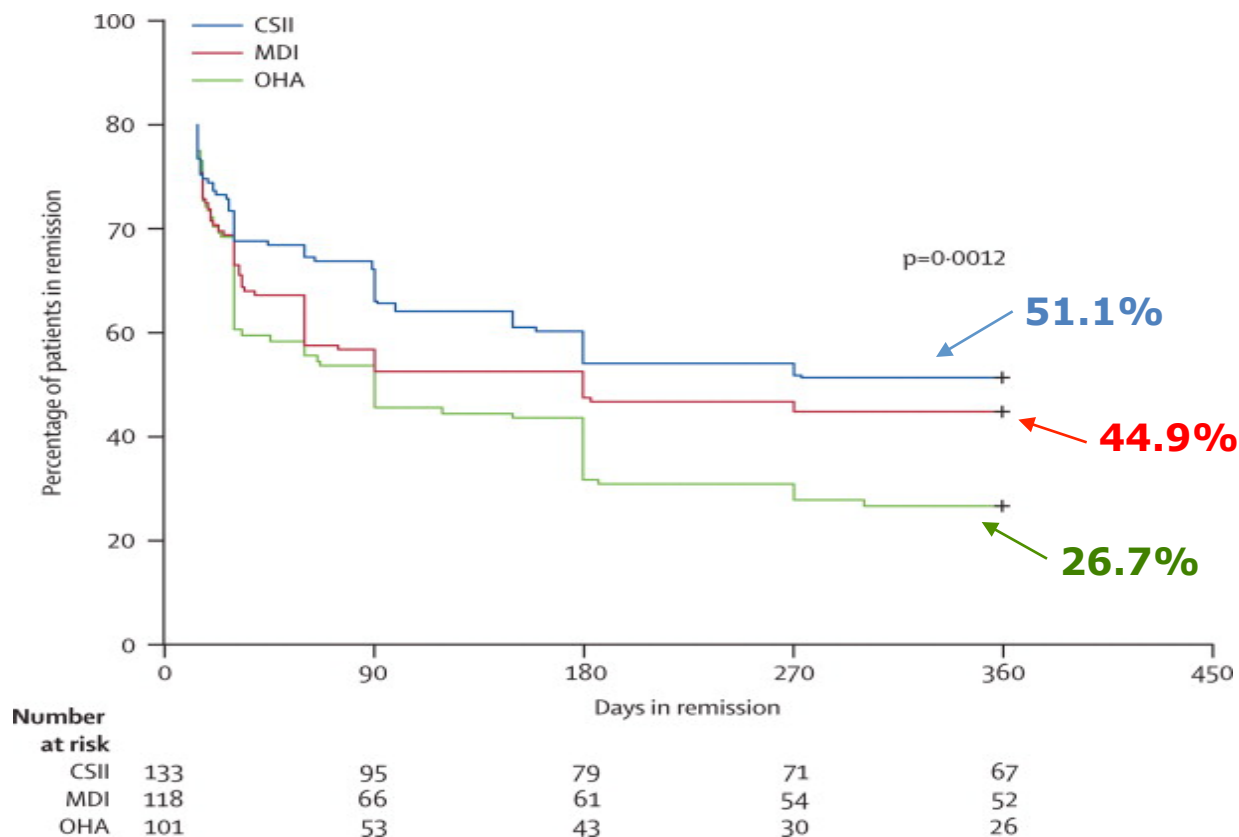
Riduzione degli Episodi Ipoglicemici Lispro vs. Regolare (Diabete Tipo 1)



Azione fisiologica



Effetto della terapia insulinica intensiva sulla funzione β -cellulare e sul controllo glicemico in diabetici tipo 2 di nuova diagnosi



Effetti vascolari dell'insulina

Vasodilatazione Effetto cardioprotettivo

In

Diabetes Care. 2013 Sep;36(9):2466-74. doi: 10.2337/dc12-2129. Epub 2013 Apr 5.

Effect of insulin glargine and n-3FA on carotid intima-media thickness in people with dysglycemia at high risk for cardiovascular events: the glucose reduction and atherosclerosis continuing evaluation study (ORIGIN-GRACE).

Lonn EM1, Bosch J, Diaz R, Lopez-Jaramillo P, Ramachandran A, Hancu N, Hanefeld M, Krum H, Ryden L, Smith S, McQueen MJ, Dyal L, Yusuf S, Gerstein HC; GRACE and ORIGIN Investigators.

↓ produzione di ROS

↓ NFκB

↓ TF

↓ PAI-1

↓

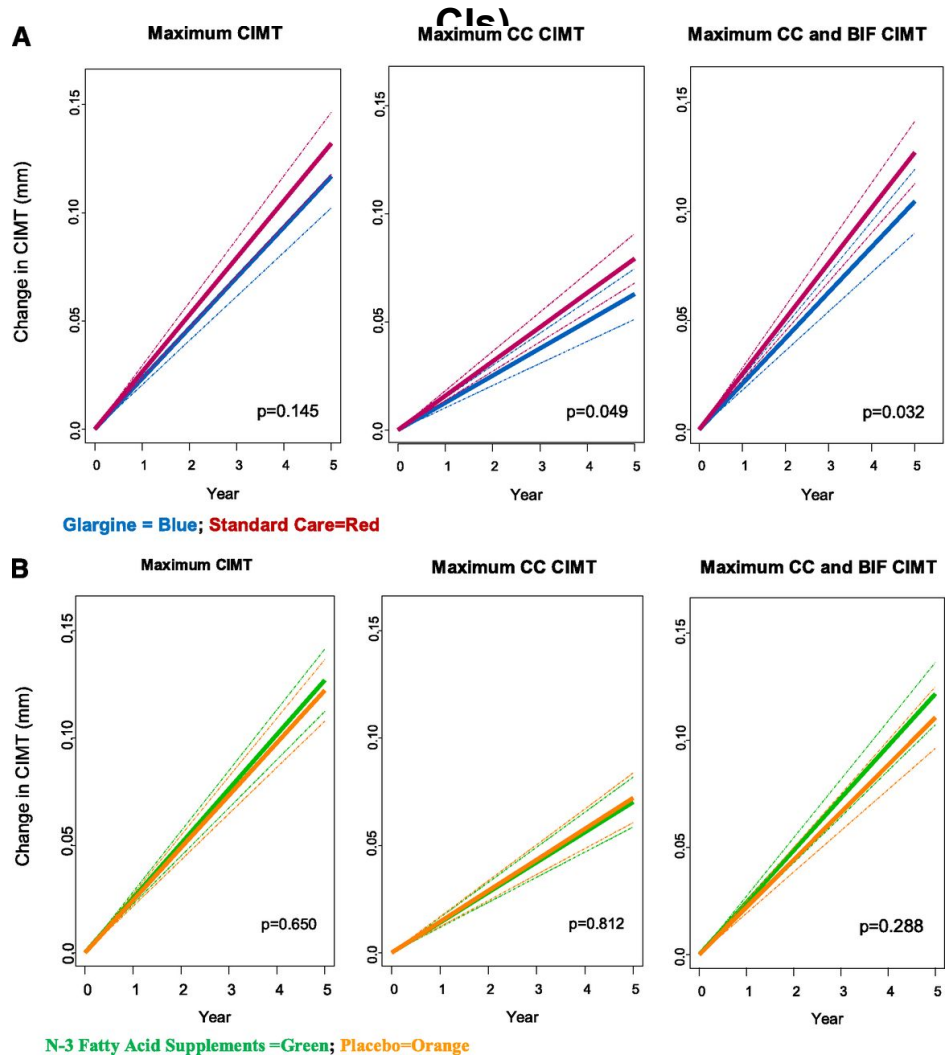
↓ MCP

↓ ICAM-1

↓ CRP

Anti-
aterosclerotico

Changes in the primary and secondary CIMT outcomes by treatment group for the insulin glargine (A) and n-3FA (B) arms of the trial (slopes of carotid intima-media change and 95% CI)



The Glucose Reduction and Atherosclerosis Continuing Evaluation Study (ORIGIN-GRACE)

Lonn E M et al. Dia Care 2013;36:2466-2474

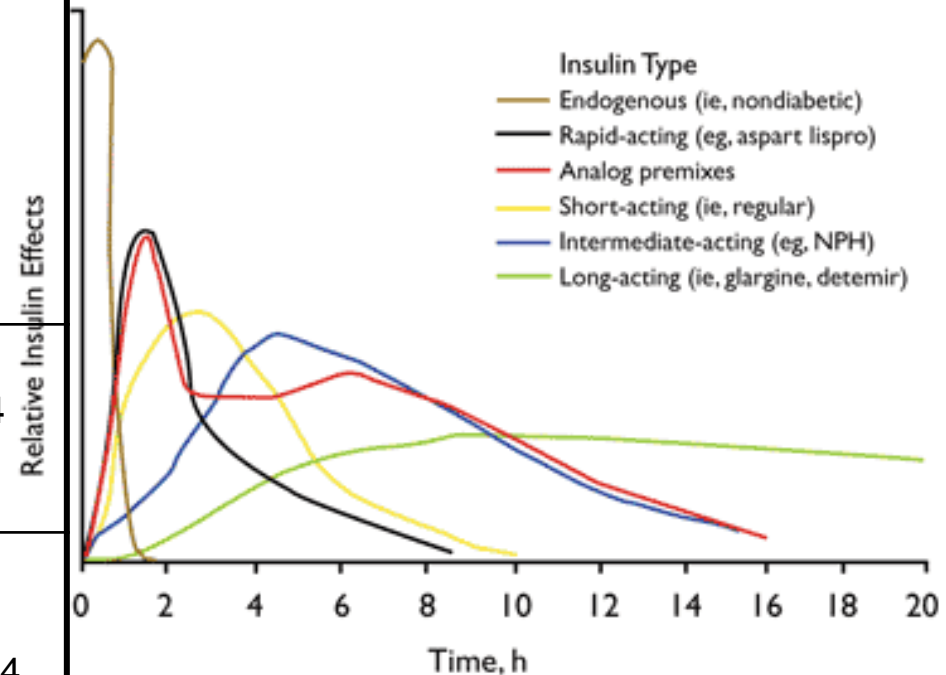


flessibilità di trattamento

- Differenze nell'inizio, nel picco, durata d'azione

Profilo farmadocinamico - insulina umana e analoghi rapidi

	inizio (h)	Picco (h)	Durata (h)
Rapida			
RHI	0.5–1	2.5–5	8–12
Lispro	0.25–	0.5–1.5	2–5
Aspart	0.5	1–3	3–5
Glulisine	0.17– 0.33 0.25	0.5–1.5	1–2.5
Lispro protaminata	1–1.5	6–14	16–24
Lenta			
Glargine	1.1	–	24
Detemir	0.8–2	–	up to 24



Confronto fra gli analoghi rapidi dell'insulina umana

RCP e Position Statement



Con riferimento all'applicazione del principio di equivalenza per gli analoghi rapidi dell'insulina glulisina (Apidra®), lispro (Humalog®) e aspart (NovoRapid®), la Società Italiana di Diabetologia (SID), la Associazione Medici Diabetologi (AMD) e la Società Italiana di Endocrinologia e Diabetologia Pediatrica (SIEDP), esprimono il seguente parere:

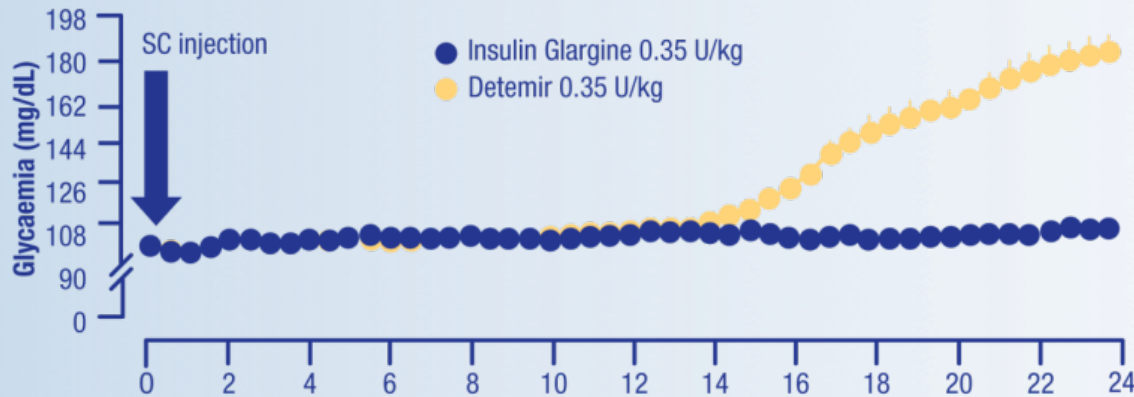
Ad oggi
dimostrato

- **Non ci sono dati certi di sicurezza per GLULISINA in bambini < 6aa, anziani, gravidanza, allattamento**
- **LISPRO la più sicura in IRC ed Insuff. epatica gravi**

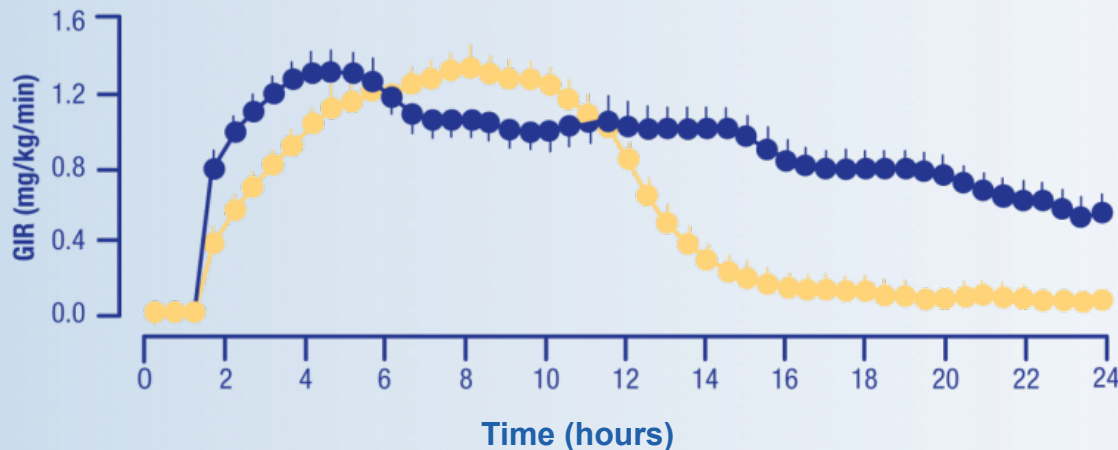
e che
spart

FARMACODINAMICA – CONFRONTO

insulina glargina and detemir



**Tempo medio di durata
d'azione 24 ore e 17.5 per
glargina vs detemir,
($p < 0.001$)**



**Tasso di infusione di
glucosio è simile per le
prime 12 ore,
successivamente c'è una
diminuzione molto più
rapida con detemir
($p < 0.001$)**

Comparison of the Efficacy and Safety of Insulin Glargine and Insulin Detemir with NPH Insulin in Children and Adolescents with Type 1 Diabetes Mellitus Receiving Intensive Insulin Therapy

[Bumin Nuri Dünder](#),¹ [Nihal Dünder](#),² and [Erdal Eren](#)³

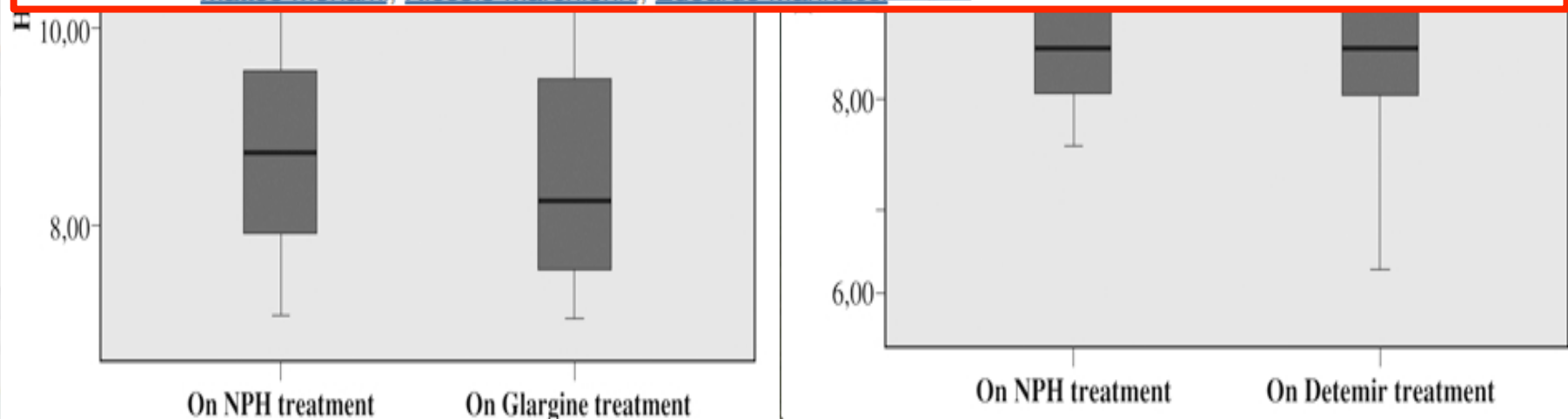
Diabetes Research and Clinical Practice

[Volume 81, Issue 2](#), Pages 184-189, August 2008

Long-acting insulin analogues versus NPH human insulin in type 2 diabetes:

A meta-analysis

• [Matteo Monami](#), [Niccolò Marchionni](#), [Edoardo Mannucci](#)



N. Engl. J. Med. 2012 Jul 26;367(4):319-28. doi: 10.1056/NEJMoa1203858. Epub 2012 Jun 11.

Basal insulin and cardiovascular and other outcomes in dysglycemia.

ORIGIN_Trial Investigators, Gerstein HC, Bosch J, Dagenais GR, Díaz B, Jung H, Maggioni AP, Pogue J, Probstfield J, Ramachandran A, Riddle MC, Rydén LE, Yusuf S.

Collaborators (27)

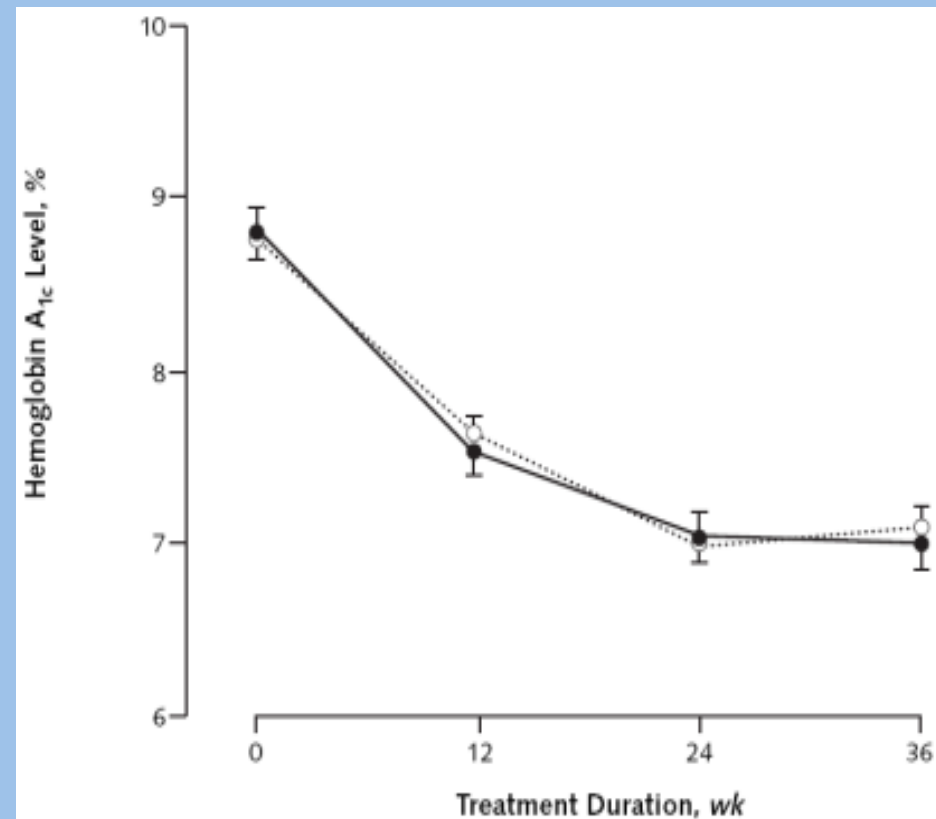
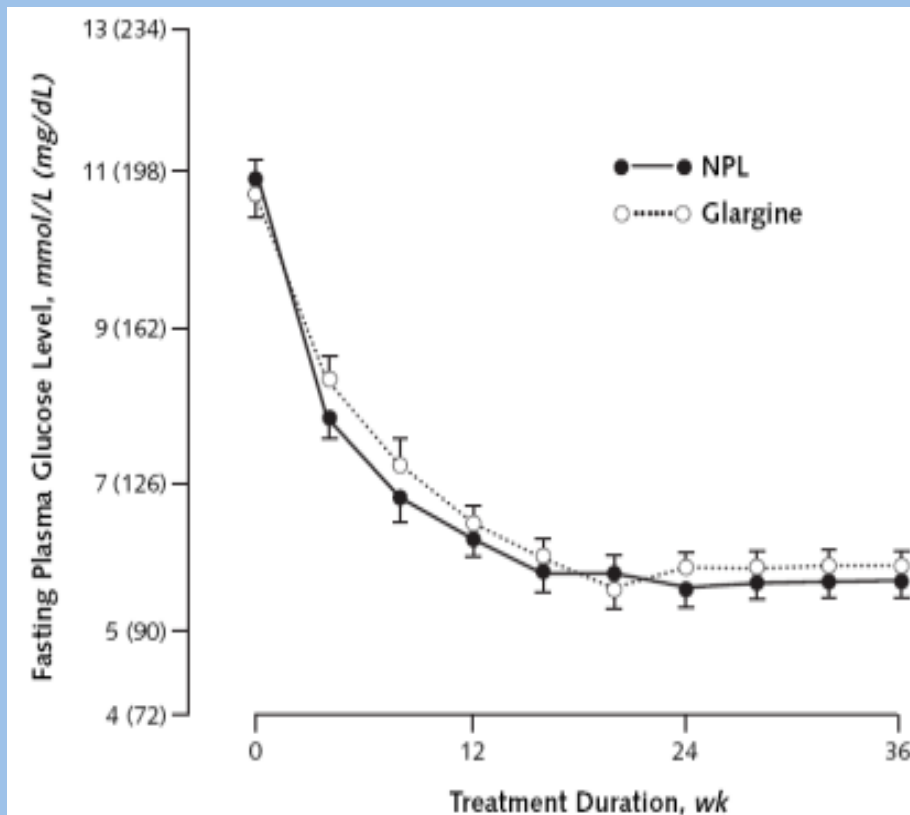
In basse dosi (0,3 U/kg/die) non si associa ad aumento di rischio neoplastico

Abstract

BACKGROUND:

The provision of sufficient basal insulin to normalize fasting plasma glucose levels may reduce cardiovascular events, but such a possibility has not been formally tested.

Lispro-Protamina vs Glargine nel T2DM: effetti sui livelli di glicemia a digiuno e HbA1c



Studio randomizzato, in aperto; 36 settimane, 116 pz con T2DM

Basal Supplementation of Insulin Lispro Protamine Suspension Versus Insulin Glargine and Detemir for Type 2 Diabetes

Meta-analysis of randomized controlled trials

- . Katherine Esposito, MD, PHD¹↓, Paolo Chiodini, MSC², Annalisa Capuano, MD³, Michela Petrizzo, MD⁴, Maria Rosaria Improta, MD⁴ and Dario Giugliano, MD, PHD⁴**
+

In conclusion, our analyses suggest that there is no clinically relevant difference in the efficacy of ILPS versus insulin glargine or detemir for targeting hyperglycemia, but ILPS was associated with more nocturnal hypoglycemia than comparators. The comparison of ILPS with insulin glargine or detemir using a once-daily dosing regimen shows a nonsignificant difference in HbA_{1c} change from baseline and hypoglycemia.

Efficacy and safety of degludec insulin: a meta-analysis of randomised trials.

Monami M1, Mannucci E.

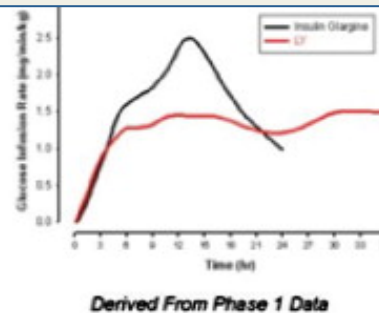
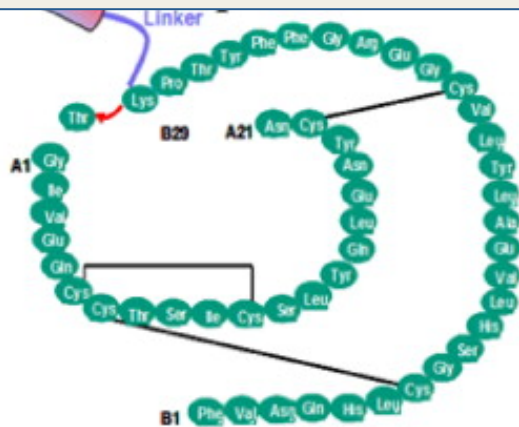


A Randomized, Controlled Study of Once Daily LY2605541, a Novel Long-Acting Basal Insulin, Versus Insulin Glargine in Basal Insulin-Treated Patients With Type 2 Diabetes.

Bergenstal RM, Rosenstock J et al.

Diabetes Care. 2012 Jul 11. [Epub ahead of print]

LY2605541 similarly improves glucose control compared to insulin glargine, but with
Weight loss,
Less nocturnal hypoglycemia, and
Less intraday glycemic variability



- Less patient variability
- Less hypoglycemia risk
- Better patient control

Status: Phase 1 studies

(b)

Segretagoghi: Sulfanilure e Glinidi

Vantaggi

- Efficacia ipoglicemizzante

Svantaggi

- Ipoglicemie

[Diabetes Res Clin Pract](#), 2008 Feb;79(2):196-203. Epub 2007 Oct 10.

Comparison of different drugs as add-on treatments to metformin in type 2 diabetes: a meta-analysis.

[Monami M1](#), [Lamanna C](#), [Marchionni N](#), [Mannucci E](#).

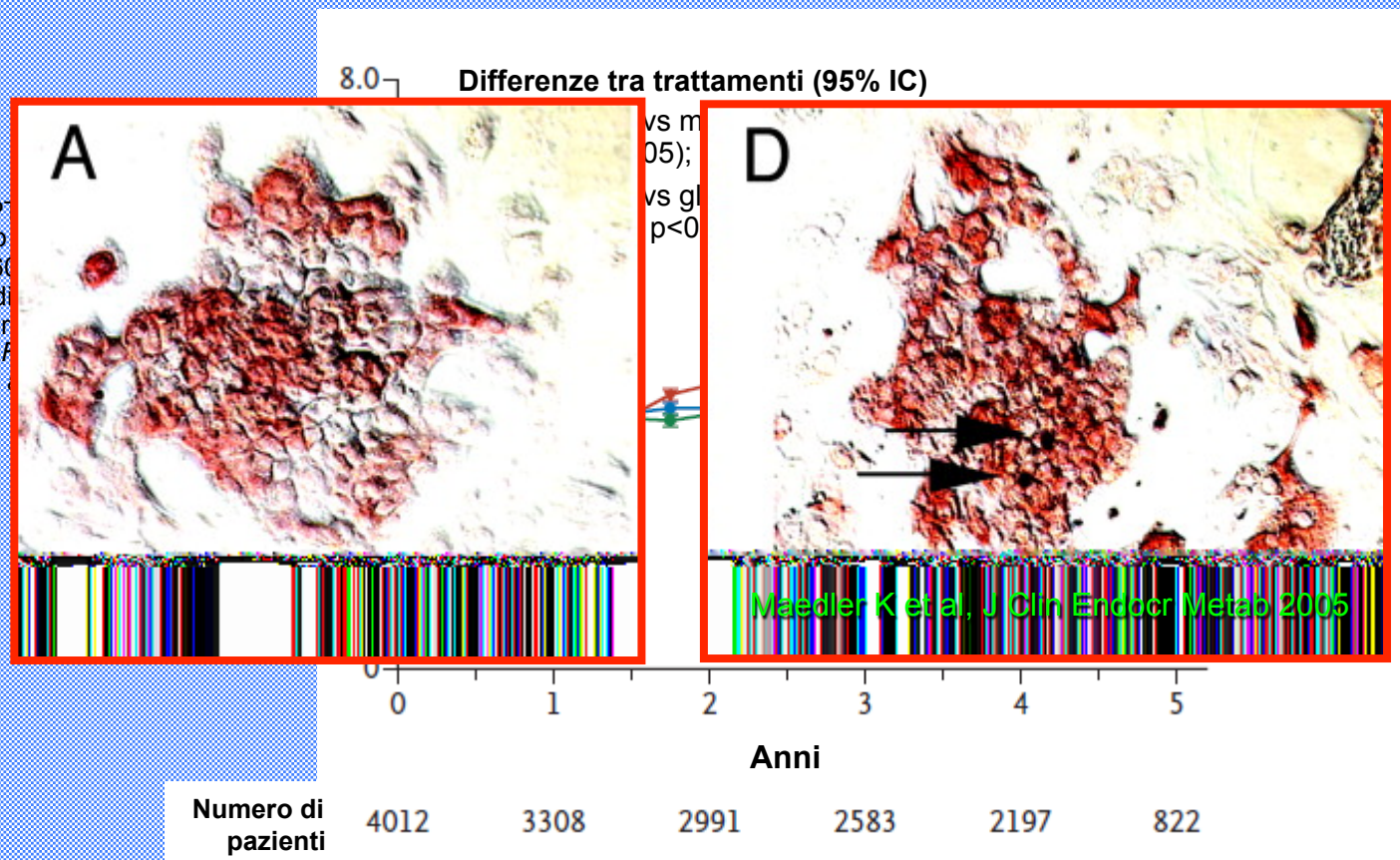
Maggior riduzione HbA1C rispetto acarbiosio e glitazoni, con effetto simile all' insulina

- No IRC (solo glinide VFG < 30)
- Possibile effetto negativo nel recupero post ischemico

Variazioni dell'emoglobina glicata nel tempo

Gli indici glicemici aumentano nel tempo, probabilmente quale conseguenza del declino della funzione delle β -cellule

Studio ADOPT randomizzato cieco, in 4.360 con diabete di tipo 2 precedentemente trattati con insulina. L'età mediana di 4...



[Diabetes Obes Metab](#). 2013 Oct;15(10):938-53. doi: 10.1111/dom.12116. Epub 2013 May 13.

Cardiovascular safety of sulfonylureas: a meta-analysis of randomized clinical trials.

[Monami M](#)1, [Genovese S](#), [Mannucci E](#).

CONCLUSIONS:

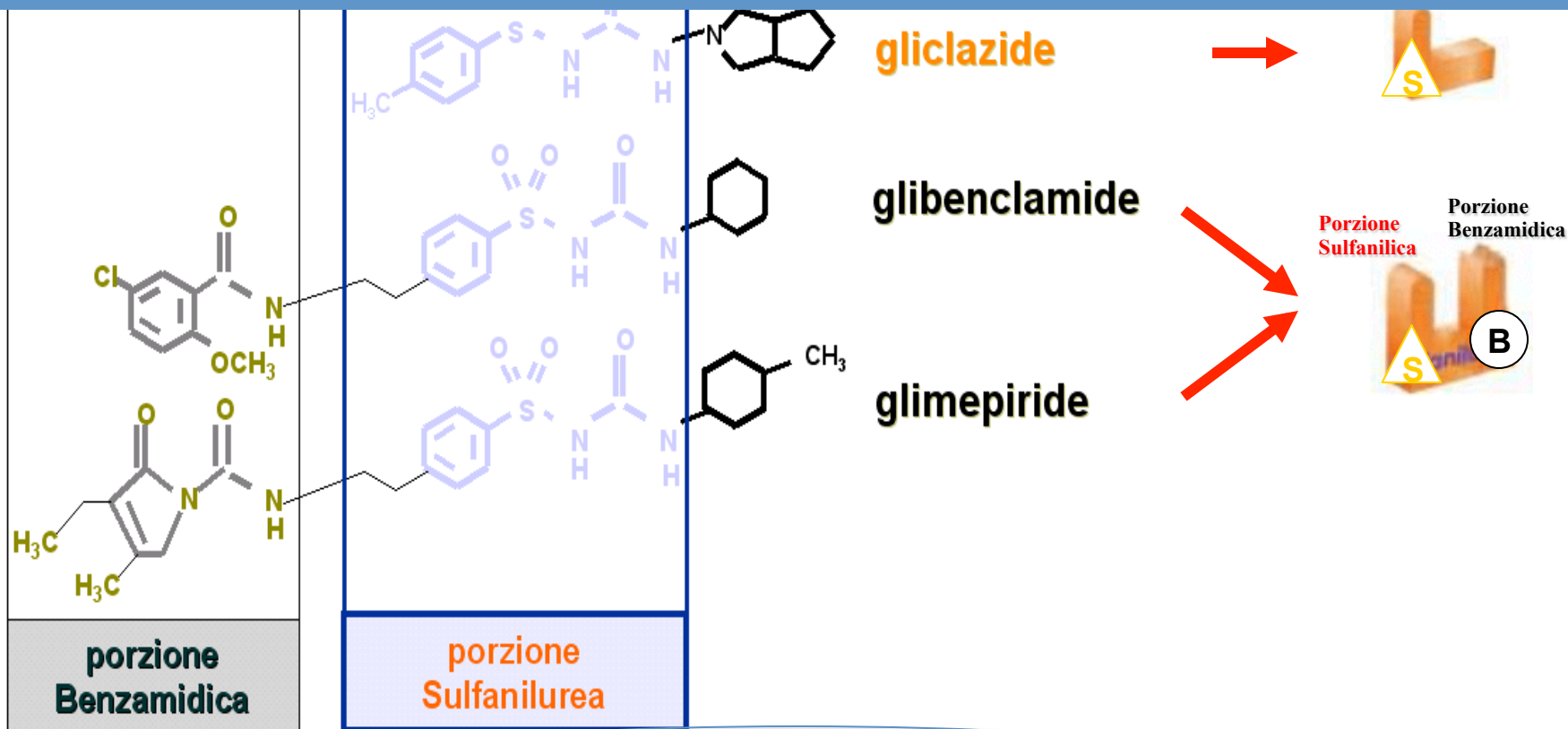
In type 2 diabetes, the use of sulfonylureas is associated with increased mortality and a higher risk of stroke, whereas the overall incidence of MACE appears to be unaffected. Significant differences in cardiovascular risk could be present in direct comparisons with specific classes of glucose-lowering agents, such as DPP4 inhibitors, but this hypothesis needs to be confirmed in long-term cardiovascular outcomes trials. The results of this meta-analysis need to be interpreted with caution, mainly because of limitations in trial quality and under-reporting of information on cardiovascular events and mortality. However, the cardiovascular safety of sulfonylureas cannot be considered established unless it is evaluated in long-term cardiovascular outcomes trials.

Diabetologia. 1999 Jul;42(7):845-8.

Differential sensitivity of beta-cell and extrapancreatic K(ATP) channels to gliclazide.

Gribble FM1, Ashcroft FM.

Author information



Selettività e reversibilità di legame

Tiazolidinedioni

Vantaggi

- Durability
- No ipoglicemia

Svantaggi

- Aumento ponderale
- Ritenzione idrica

BMC Endocr Disord. 2009 Jul 29;9:17. doi: 10.1186/1472-6823-9-17.

Actos Now for the prevention of diabetes (ACT NOW) study.

DeFronzo RA1, Banerji M, Bray GA, Buchanan TA, Clement S, Henry RR, Kitabchi AE, Mudaliar S, Musi N, Ratner R, Reaven PD, Schwenke D, Stentz FB, Tripathy D.

- No insufficienza epatica e scompenso cardiaco

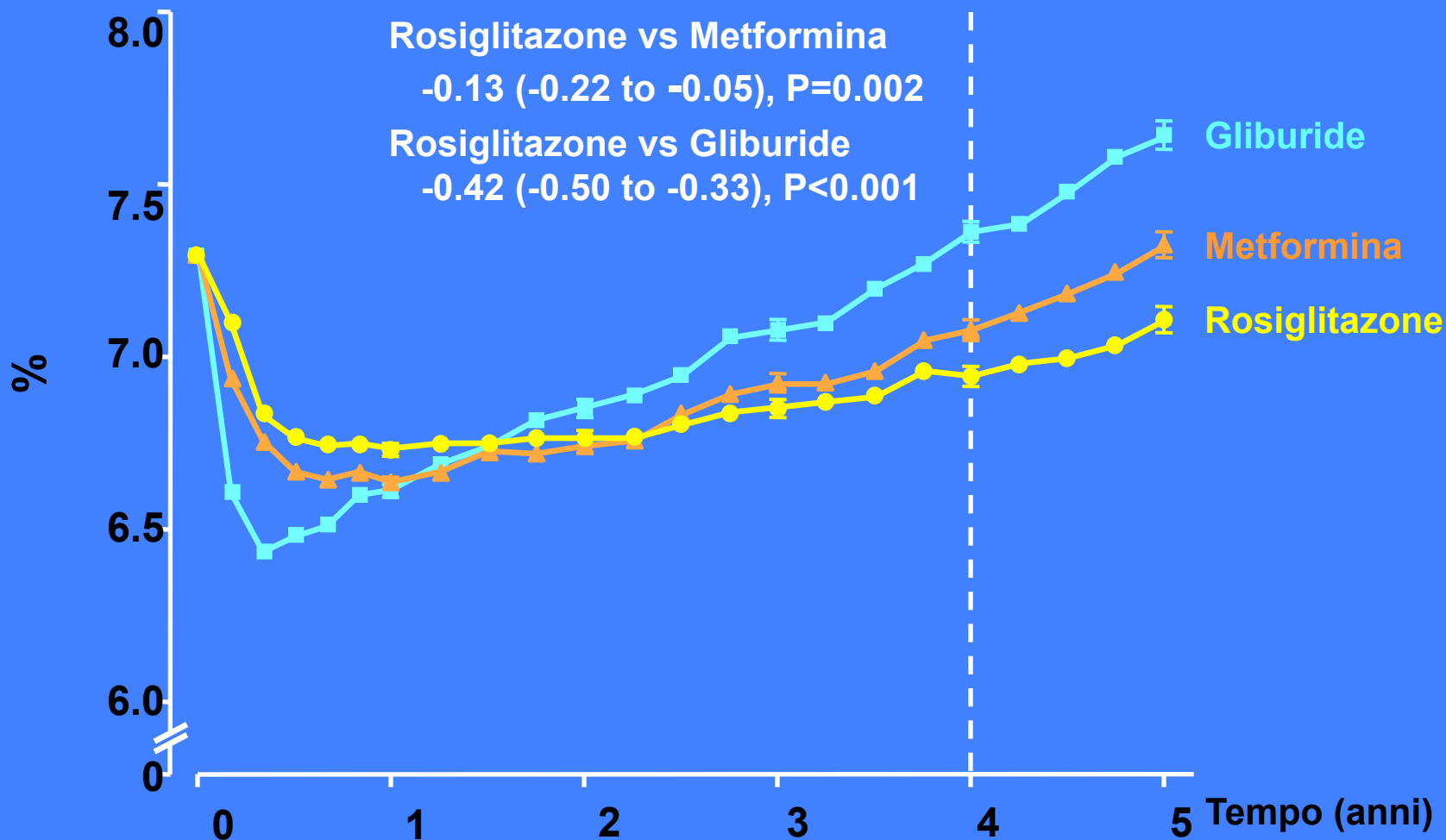
Diabetes Care. 2002 Oct;25(10):1737-43.

A diabetes outcome progression trial (ADOPT): an international multicenter study of the comparative efficacy of rosiglitazone, glyburide, and metformin in recently diagnosed type 2 diabetes.

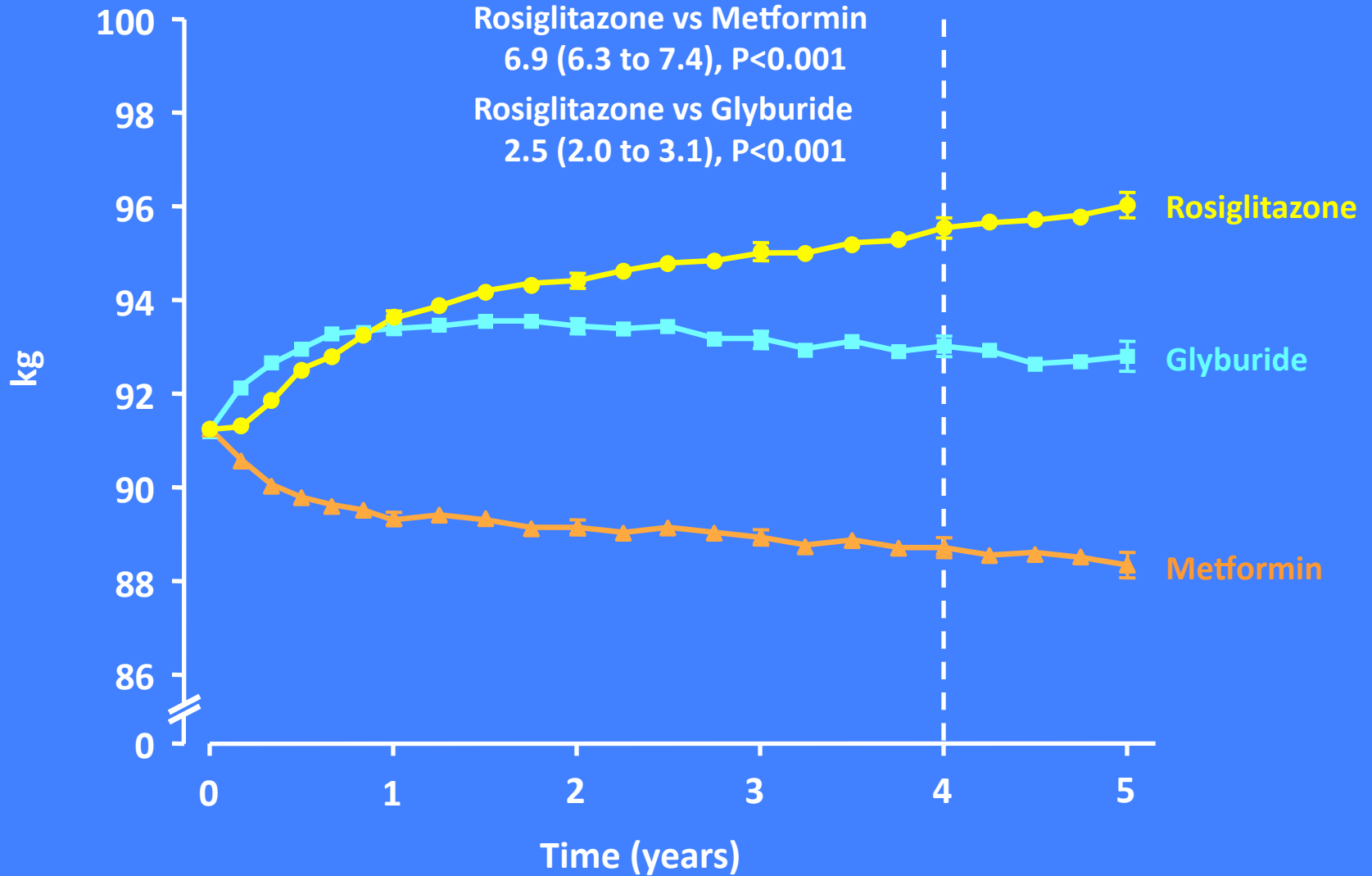
Viberti G¹, Kahn SE, Greene DA, Herman WH, Zinman B, Holman RR, Haffner SM, Levy D, Lachin JM, Berry RA, Heise MA, Jones NP, Freed MI.

Studio ADOPT

HbA1c nel Tempo



Weight Over Time



Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial

	n (%)	n (%)
Interpretation		
Pioglitazone reduces the composite of all-cause mortality, non-fatal myocardial infarction, and stroke in patients with type 2 diabetes who have a high risk of macrovascular events.		
Swelling in the absence of heart failure	502 (21.0)	541 (19.0)
NSAE leading to permanent cessation	136 (5.2)	94 (3.6)
Weight gain leading to permanent cessation	21 (0.8)	6 (0.2)
Any NSAE of special interest	1230 (47.2)	886 (33.6)
Other NSAEs	1538 (59.0)	1566 (59.5)

N Engl J Med. 2007 Jun 14;356(24):2457-71. Epub 2007 May 21.

Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes.

Nissen SE¹, Wolski K.

RESULTS:

Data were combined by means of a fixed-effects model. In the 42 trials, the mean age of the subjects was approximately 56 years, and the mean baseline glycosylated hemoglobin level was approximately 8.2%. In the rosiglitazone group, as compared with the control group, the odds ratio for myocardial infarction was 1.43 (95% confidence interval [CI], 1.03 to 1.98; P=0.03), and the odds ratio for death from cardiovascular causes was 1.64 (95% CI, 0.98 to 2.74; P=0.06).

CONCLUSIONS:

Rosiglitazone was associated with a significant increase in the risk of myocardial infarction and with an increase in

Acarbosio

Vantaggi

- Sicurezza
- Prevenzione diabete

Svantaggi

- Meteorismo e flatulenza
- Non rimborsabilità
- Efficacia inferiore (0,7-0,9 punti percentuali)

Diabetes Care. 1998 Oct;21(10):1720-5.

The STOP-NIDDM Trial: an international study on the efficacy of an alpha-glucosidase inhibitor to prevent type 2 diabetes in a population with impaired glucose tolerance: rationale, design, and preliminary screening data. Study to Prevent Non-Insulin-Dependent Diabetes Mellitus.

Chiasson JL, Gomis R, Hanefeld M, Josse RG, Karasik A, Laakso M.

[Diabet Med.](#) 2008 Apr;25(4):435-41. doi: 10.1111/j.1464-5491.2008.02391.x. Epub 2008 Mar 13.

Comparison of vildagliptin and acarbose monotherapy in patients with Type 2 diabetes: a 24-week, double-blind, randomized trial.

Pan C¹, Yang W, Barona JP, Wang Y, Niggli M, Mohideen P, Wang Y, Foley JE.

Diabetes Care. 2014 May;37(5):1338-45. doi: 10.2337/dc13-1901. Epub 2014 Feb 26.

Second-line agents for glycemic control for type 2 diabetes: are newer agents better?

Zhang Y1, McCoy RG, Mason JE, Smith SA, Shah ND, Denton BT.

Author information

Abstract

OBJECTIVE While metformin is generally accepted as the first-line agent in treatment of type 2 diabetes, there are insufficient evidence and extensive debate about the best second-line agent. We aimed to assess the benefits and harms of four

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RESULTS Acc

CONCLUSIONS

Use of sulfonylurea as second-line therapy for type 2 diabetes generated glycemic control and QALYs comparable with those associated with other agents but at lower cost. A model that incorporates HbA1c and diabetes complications can serve as a useful clinical decision tool for selection of treatment options.

quality of life, glycemic using a U.S. sification of eptor agonist, to insulin chemic heart death. nic control
goal, but the regimen with sulfonylurea incurred significantly lower cost per QALY and resulted in the longest time to insulin dependence. An HbA1c goal of 7% (53 mmol/mol) produced higher QALYs compared with a goal of 8% (64 mmol/mol) for all regimens. **CONCLUSIONS** Use of sulfonylurea as second-line therapy for type 2 diabetes generated glycemic control and QALYs comparable with those associated with other agents but at lower cost. A model that incorporates HbA1c and diabetes complications can serve as a useful clinical decision tool for selection of treatment options.

Terapia personalizzata e flessibile

