Quali nuove opzioni terapeutiche dai Farmaci anti-iperglicemizzanti “tradizionali” ?

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Gli antidiabetici orali
i farmaci "tradizionali"

Insulino-sensibilizzanti

Metformina

Glitazoni

Secretagoghi

Sulfoniluree

Glinidi

Modificatori dell'assorbimento intestinale

Inibitori dell'α-Glucosidasi intestinale

UK
NICE guidelines

2002

Metformina : prima linea per il paziente sovrappeso e NORMOPESO

1st global guidelines IDF

2005

Metformina : prima linea, indipendentemente dal peso corporeo

ADA / EASD Consensus

2006

Metformina: alla diagnosi, in aggiunta all'intervento sullo stile di vita

ADA Consensus

2007

Solo metformina dovrebbe essere presa in considerazione come trattamento farmacologico nei soggetti con IFG/IGT

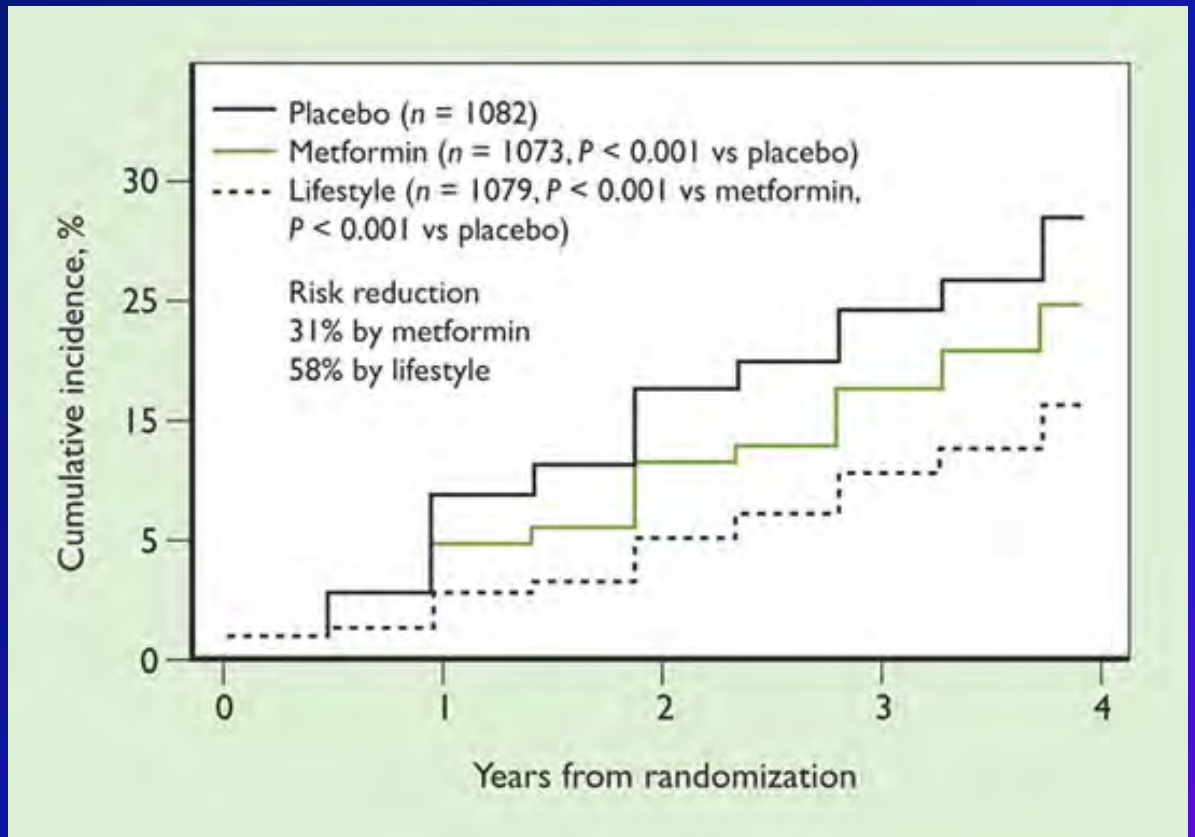
DPP: Prevenzione del diabete tipo 2

The New England
Journal of Medicine

VOLUME 346 FEBRUARY 7, 2002 NUMBER 6

REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN

DIABETES PREVENTION PROGRAM RESEARCH GROUP*



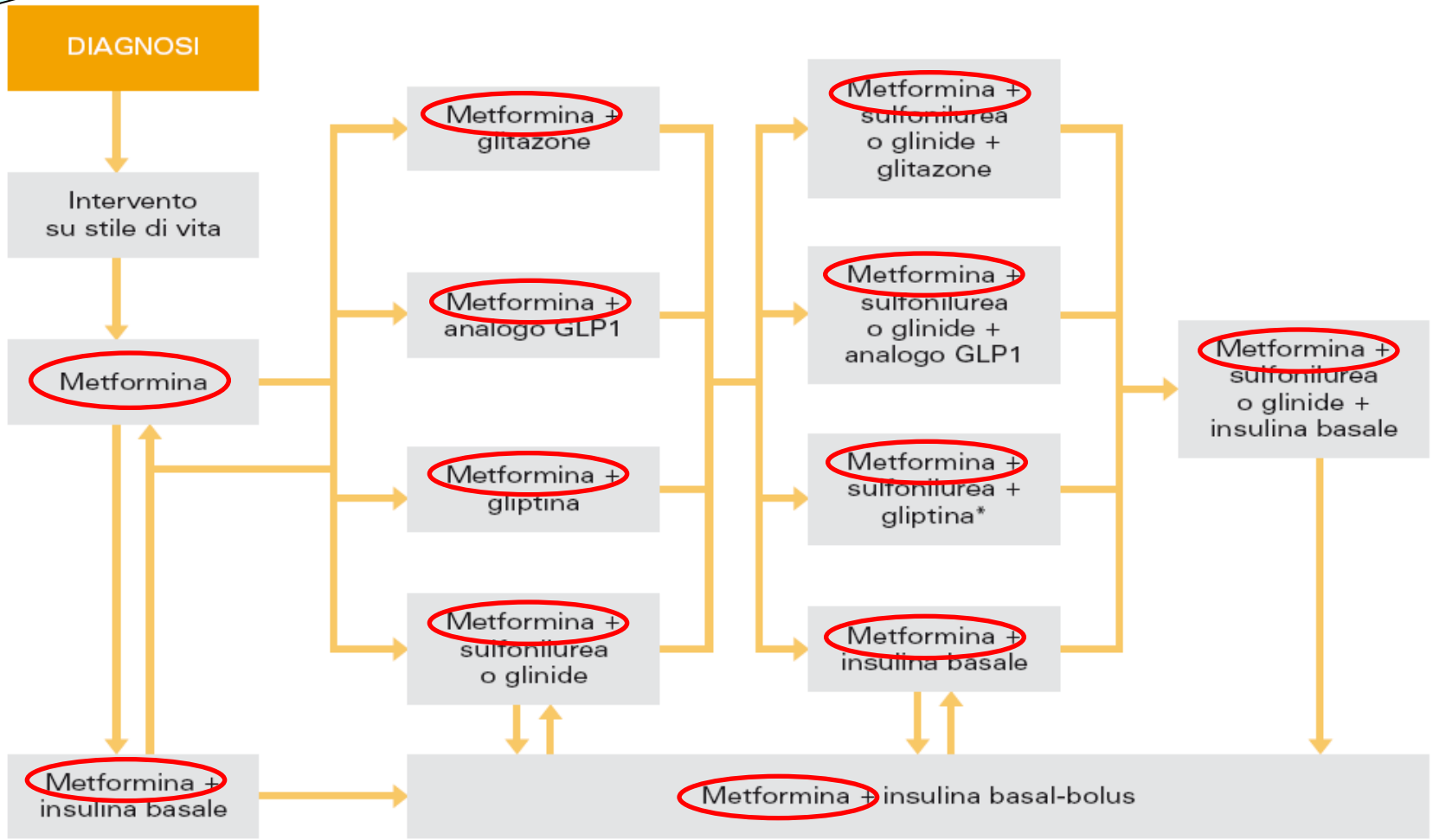
RCT;

3234 pazienti obesi con IGT/IFG;

2.8 anni

2010

per la terapia del diabete mellito di tipo 2.



In presenza di un fallimento della terapia iniziale volta a modificare lo stile di vita, prescrivere metformina, che dovrà accompagnare sempre, se tollerata e non controindicata, ogni altro farmaco, alla dose di almeno 2 g/die.

- In presenza di valori di HbA_{1c} superiori all'obiettivo glicemico è necessario mettere tempestivamente in atto le opportune variazioni della terapia finalizzate a raggiungere e mantenere nel tempo il buon controllo glicemico. (**Livello della prova II, Forza della raccomandazione B**)

- Il farmaco di prima scelta per il trattamento dei diabetici tipo 2 è la metformina: in presenza di sovrappeso (**Livello della prova II, Forza della raccomandazione A**) e di normopeso (**Livello della prova VI, Forza della raccomandazione B**)

- Metiormina, glitazoni, sulfoniluree, repaglinide, inibitori DPP-4 e analoghi del GLP-1 sono parimenti efficaci nel ridurre l'emoglobina glicosilata, ma meno efficaci rispetto all'insulina. (**Livello della prova I, Forza della raccomandazione A**)

- In molti pazienti, non in buon controllo in monoterapia, è necessario associare due o più farmaci. (**Livello della prova I, Forza della raccomandazione A**)

- Quando il controllo della glicemia non è soddisfacente, anche in politerapia, è necessario iniziare la terapia insulinica mono- o multiiniettiva. (**Livello della prova I, Forza della raccomandazione A**)

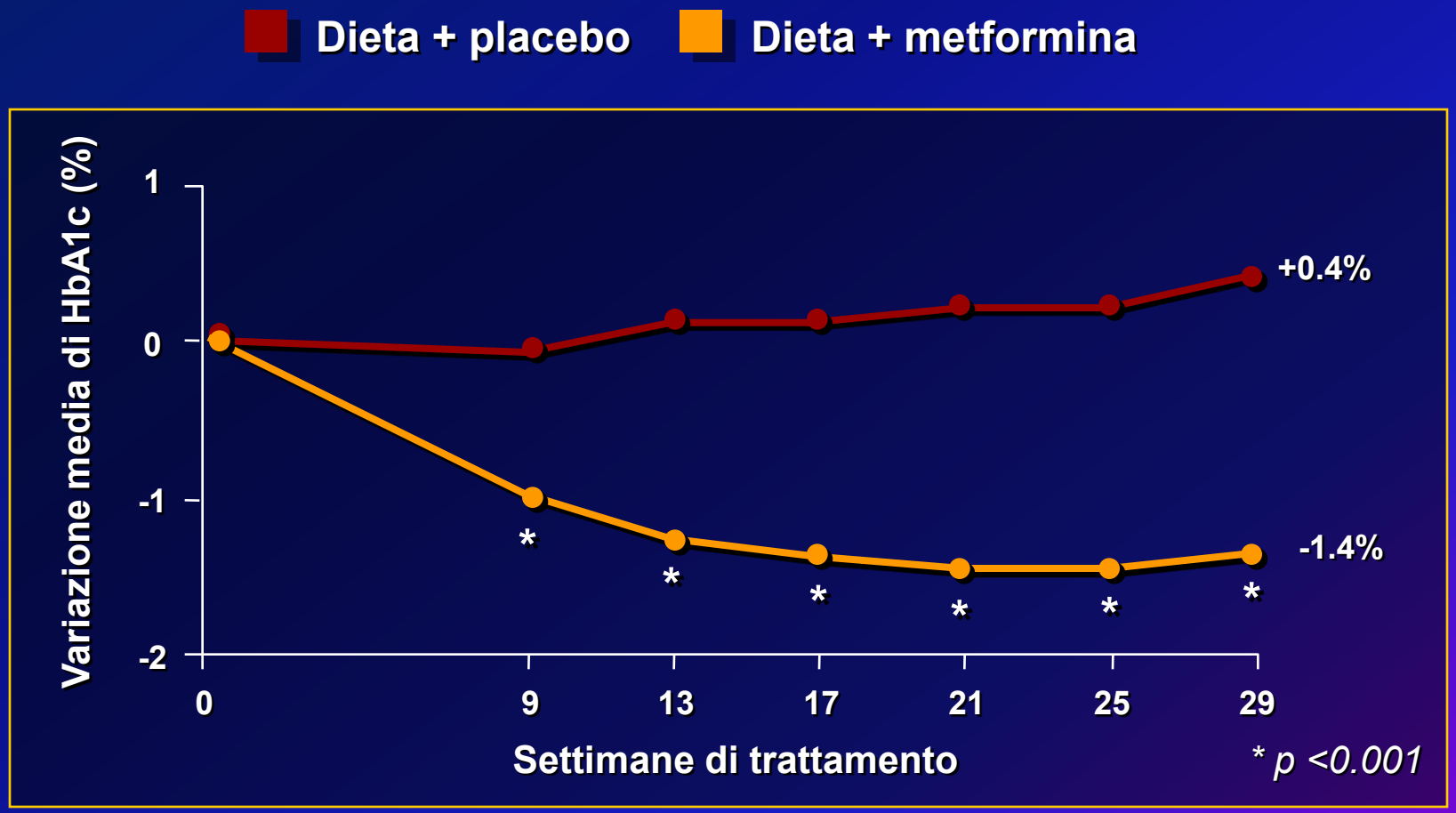
- Tenere in considerazione la possibile scarsa adesione alla terapia prescritta. (**Livello della prova I, Forza della raccomandazione A**)

Intervenire

Il trattamento del diabete deve essere tempestivamente adattato in ogni paziente fino a ottenere valori di HbA1c stabilmente inferiori a 7% (Tabella 9bis), valori che consentono di prevenire l'incidenza e la progressione delle complicanze microvascolari.

(Livello della prova I, Forza della raccomandazione A).

Metformina: effetto sulla HbA1c



Mod. da De Fronzo RA, et al. N Engl J Med 1995; 333: 541-549.

UKPDS 34
Miglioramento dei parametri clinici

	Trattamento intensivo con metformina		Trattamento intensivo con sulfonilurea/insulina	
	Δ rischio*	p	Δ rischio*	p
Morti correlate al diabete	↓ 42%	0.017	↓ 20%	0.19
Mortalità da tutte le cause	↓ 36%	0.011	↓ 8%	0.49
Qualsiasi endpoint correlato al diabete	↓ 32%	0.0023	↓ 7%	0.46
Infarto del miocardio	↓ 39%	0.01	↓ 21%	0.11
Ictus	↓ 41%	0.13	↑ 14%	0.60

* Rispetto alla terapia convenzionale (gruppo sovrappeso)

Lancet (1998):352:854-865

Clinical Care/Education/Nutrition/Psychosocial Research

ORIGINAL ARTICLE

Secondary Failure of Metformin Monotherapy in Clinical Practice

JONATHAN B. BROWN, PHD, MPP[1]
CHRISTOPHER CONNER, PHARMD, PHD[2]
GREGORY A. NICHOLS, PHD[1]

OBJECTIVE — We sought to document the secondary failure rate of metformin monotherapy in a clinical practice setting and to explore factors that predict therapeutic failure.

RESEARCH DESIGN AND METHODS — We studied 1,799 type 2 diabetic patients who, between 2004 and 2006, lowered their A1C to <7% after initiating metformin monotherapy as their first-ever anti-hyperglycemic drug. We examined all A1C values recorded through 31 December 2008 (2–5 years of follow-up), defining secondary failure as a subsequent A1C ≥7.5% or the addition or substitution of another anti-hyperglycemic agent. We used logistic regression to identify factors associated with the probability of secondary failure.

RESULTS — Of the 1,799 patients studied, 42% ($n = 748$) experienced secondary failure; the mean failure rate was 17% per year. However, patients who initiated metformin within 3 months of diabetes diagnosis failed at an age-and A1C-adjusted rate of 12.2% (10.5–14.4%) per year, and patients who initiated while A1C was <7% failed at an adjusted rate of 12.3% per year. An interaction term between duration of diagnosed diabetes and A1C was not significant. Age, duration, and A1C at initiation were the only factors that predicted secondary failure.

CONCLUSIONS — Although metformin failure may occur more rapidly in clinical practice than in clinical trails, initiating it soon after diabetes diagnosis and while A1C is low might preserve β-cell function, prolong the effectiveness of metformin, reduce lifetime glycemic burden, and prevent diabetes complications. Our findings support the current treatment algorithm for hyperglycemia management that recommends metformin initiation when diabetes is first diagnosed.

Diabetes Care 33:501–506, 2010

8% to define initial success and secondary treatment failure. To our knowledge, no studies have examined the potential benefits of immediate versus delayed metformin initiation used with a modern A1C treatment threshold of 7%. Furthermore, although metformin fails at a rate of ~4% per year in clinical trials (7), the failure rate in the real world of clinical practice has not been reported.

We therefore sought to estimate the rate of secondary metformin monotherapy experienced by unselected patients in a nonresearch setting who had a documented history of successfully lowering their A1C to <7% with metformin. We then sought to identify factors associated with slower loss of glycemic control. Our observational analyses were conducted within a managed care plan using electronic medical records with substantial information technology support, including built-in alerts for A1C testing.

RESEARCH DESIGN AND METHODS

Study site

Metformina

42% di fallimento alla Metf in monoterapia in 1799 D seguiti per 5 anni : 17% anno

Ma se la Metf viene iniziata entro 3 mesi dalla presa in carico il fallimento scende al 12% all'anno.

UKPDS Post Trial

memoria metabolica

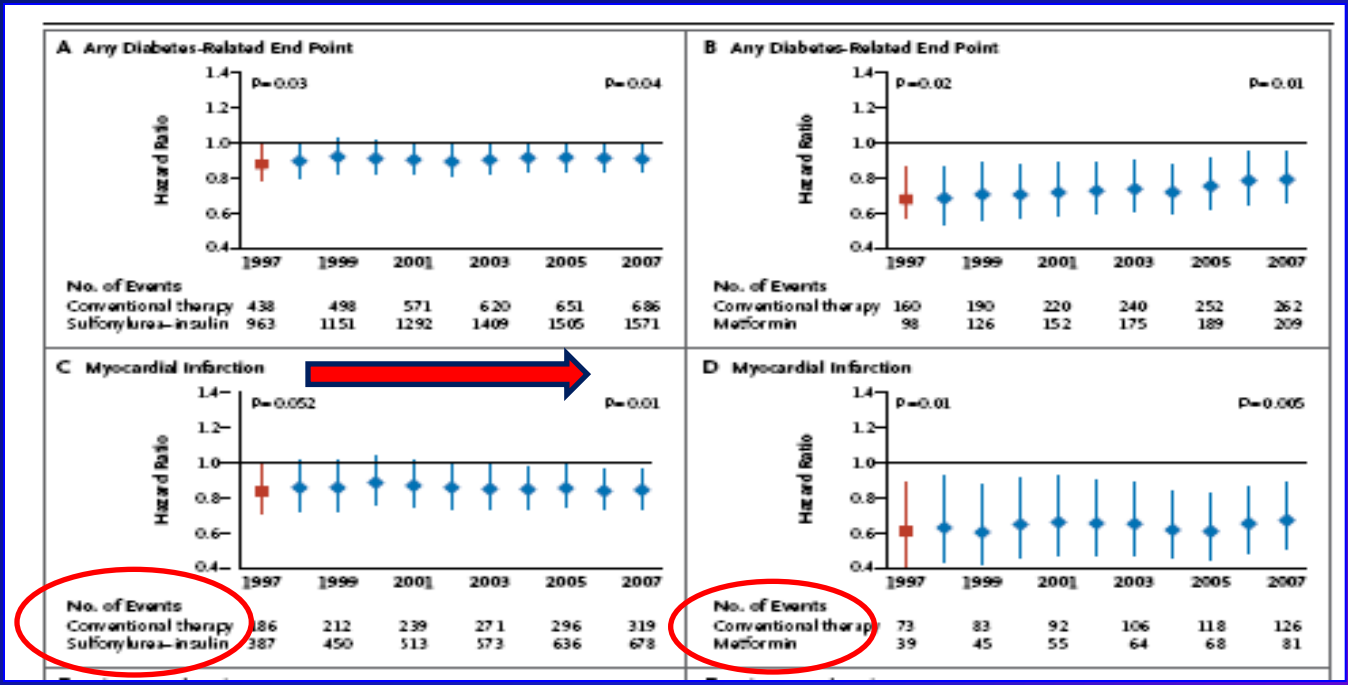
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes

Rury R. Holman, F.R.C.P., Sanjoy K. Paul, Ph.D., M. Angelyn Bethel, M.D., David R. Matthews, F.R.C.P., and H. Andrew W. Neil, F.R.C.P.

N Engl J Med 2008;359.



Follow-up a lungo termine degli studi DCCT e UKPDS suggeriscono che un trattamento volto a ottenere valori di HbA1c stabilmente inferiori a 7% subito dopo la diagnosi di diabete è associato a una riduzione a

lungo termine del

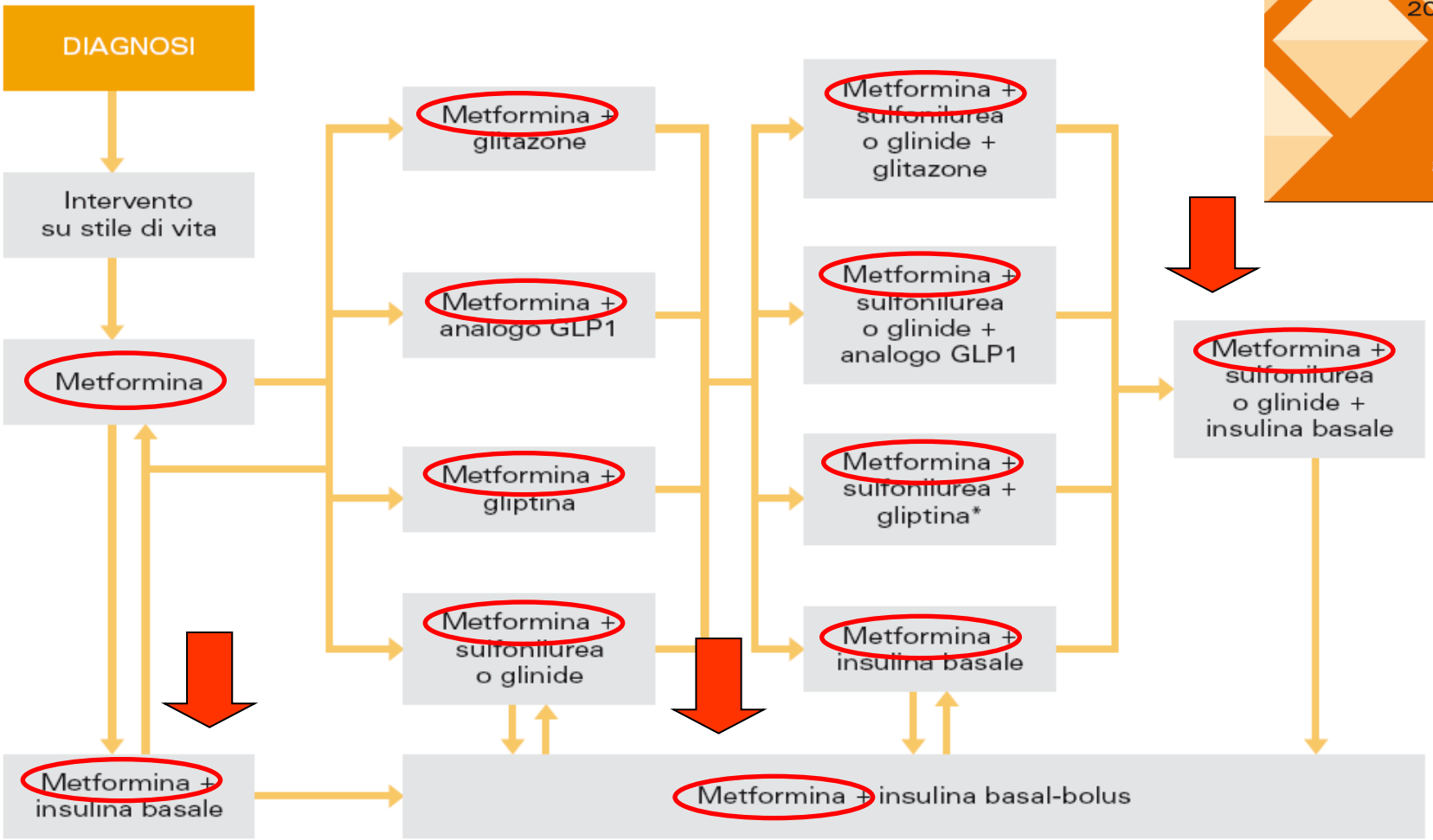
rischio di complicanze macrovascolari.

(Livello della prova III,

Forza della raccomandazione A).

METFORMINA + INSULINA

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



In presenza di un fallimento della terapia iniziale volta a modificare lo stile di vita, prescrivere metformina, che dovrà accompagnare sempre, se tollerata e non controindicata, ogni altro farmaco, alla dose di almeno 2 g/die.

Metformina : acidosi lattica e insufficienza cardiaca

- ✓ Incidenza di acidosi lattica da metformina 0-0.09 per 1000 pazienti- anno *(da fenformina 0.25- 1)*

  Salpeter, S. R. et al. Arch Intern Med 2003;163:2594-2602.

- ✓ 20-25% dei pazienti trattati con metformina ha insufficienza cardiaca

Masoudi FA et al.Metformin and thiazolidinedione use inMedicare patients with heart failure. JAMA 2003;290:81-5.
Horlen Cet al. Frequency of inappropriate metformin prescriptions. JAMA 2002;287:2504-5.
Holstein A et al.Contra-indications to metformin therapy are largely disregarded. Diabet Med 1999;16:692-6.

THE COCHRANE COLLABORATION®

Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus (Review)

Salpeter SR, Greyber E, Pasternak GA, Salpeter EE

Metformina, rispetto agli altri ipoglicemizzzanti orali, non è risultata associata ad un aumento del rischio di acidosi lattica

Objectives

To assess the incidence of fatal and nonfatal lactic acidosis, and to evaluate blood lactate levels, for those on metformin treatment compared to placebo or non-metformin therapies.

Main results

Pooled data from 347 comparative trials and cohort studies revealed no cases of fatal or nonfatal lactic acidosis in 70,490 patient-years of metformin use or in 55,451 patients-years in the non-metformin group. Using Poisson statistics the upper limit for the true incidence of lactic acidosis per 100,000 patient-years was 4.3 cases in the metformin group and 5.4 cases in the non-metformin group. There was no difference in lactate levels, either as mean treatment levels or as a net change from baseline, for metformin compared to non-metformin therapies.

Authors' conclusions

There is no evidence from prospective comparative trials or from observational cohort studies that metformin is associated with an increased risk of lactic acidosis, or with increased levels of lactate, compared to other anti-hyperglycemic treatments.

The Cochrane Library 2010, Issue 4

Proposed recommendations for use of Metformin based on eGFR

eGFR level (mL/min per 1.73m^2)	Action
≥ 60	No renal contraindication to metformin Monitor renal function annually
< 60 and ≥ 45	Continue use Increase monitoring of renal function (every 3-6 months)
< 45 and ≥ 30	Prescribe metformin with caution Use lower dose (e.g. 50%, or half-maximal dose Closely monitor renal function (every 3 months) Do not start new patients on metformin
< 30	**Stop metformin**

Additional caution is required in patients at risk for kidney injury or with anticipated significant fluctuations in renal status, based on previous history, other comorbidities, or potentially interacting medications

Lipska KJ, Bailey CJ, Inzucchi SE. Diabetes Care 2011;34:1431-37

Insufficienza cardiaca e acidosi lattica:
reali controindicazioni all'utilizzo della metformina?

1. Diabetologia 2010;53(12):2546-2553
2. Circ Heart Fail 2010 Oct 15.
3. Clin Endocrinol (Oxf) 2010 Oct 11.

Secondo questi articoli, il rischio di acidosi lattica attribuito alla metformina sarebbe largamente sovrastimato, essendo il diabete in sé, e non la terapia con il farmaco, il principale fattore di rischio per l'insorgenza di tale complicanza.

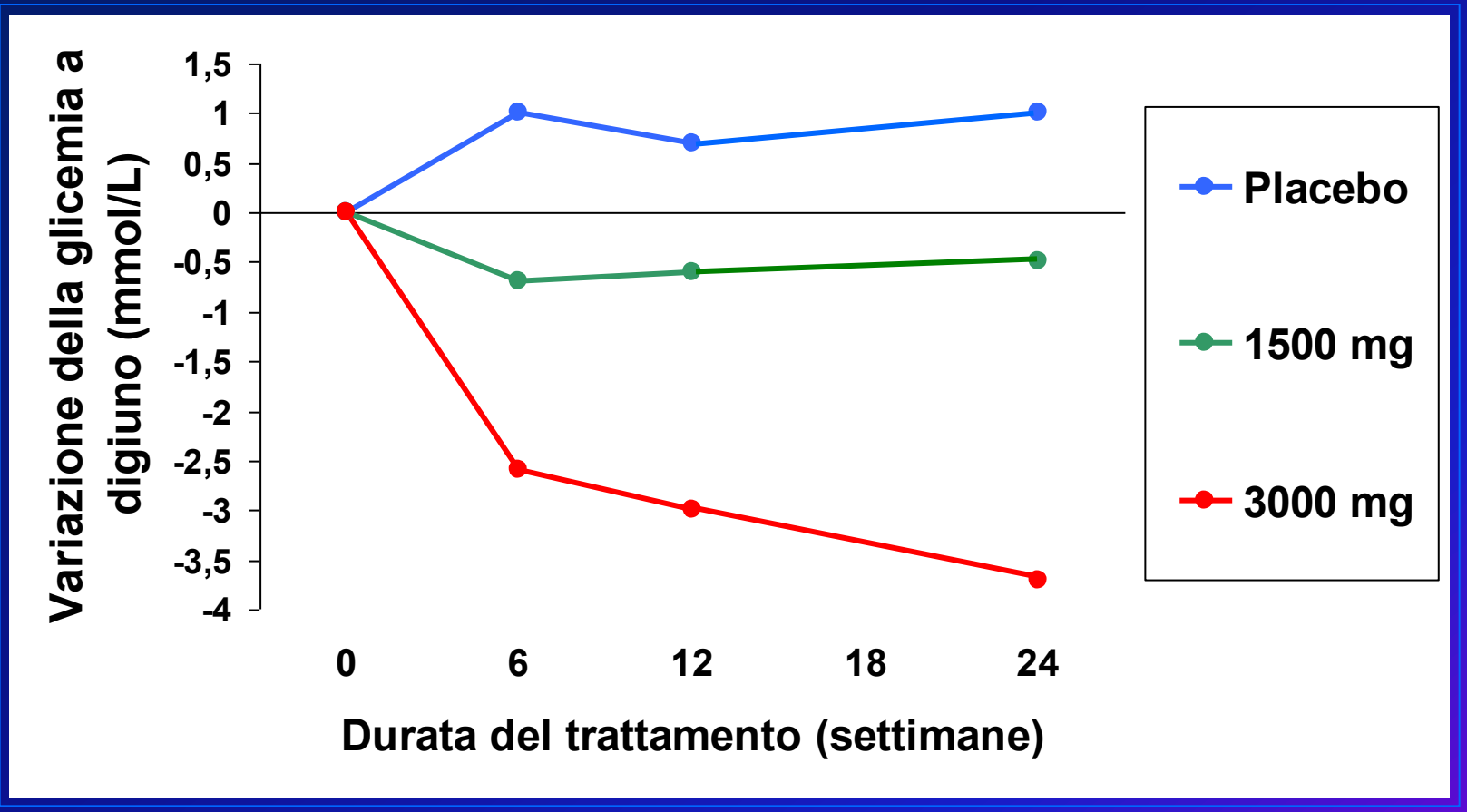
News su Thesaurus – infodiabetes.it

QUANDO NON USARLA → rischio aumentato di Ac Lattica :

- **Sepsi**
- **Insufficienza cardiaca**
- **Insufficienza respiratoria**
- **Ipossia dei tessuti**
- **Ipotensione/disidratazione**
- **Insufficienza renale acuta/cronica**
- *In caso di esami con M di Contrasto*

L'EFFICACIA DELLA METFORMINA È DOSE-CORRELATA

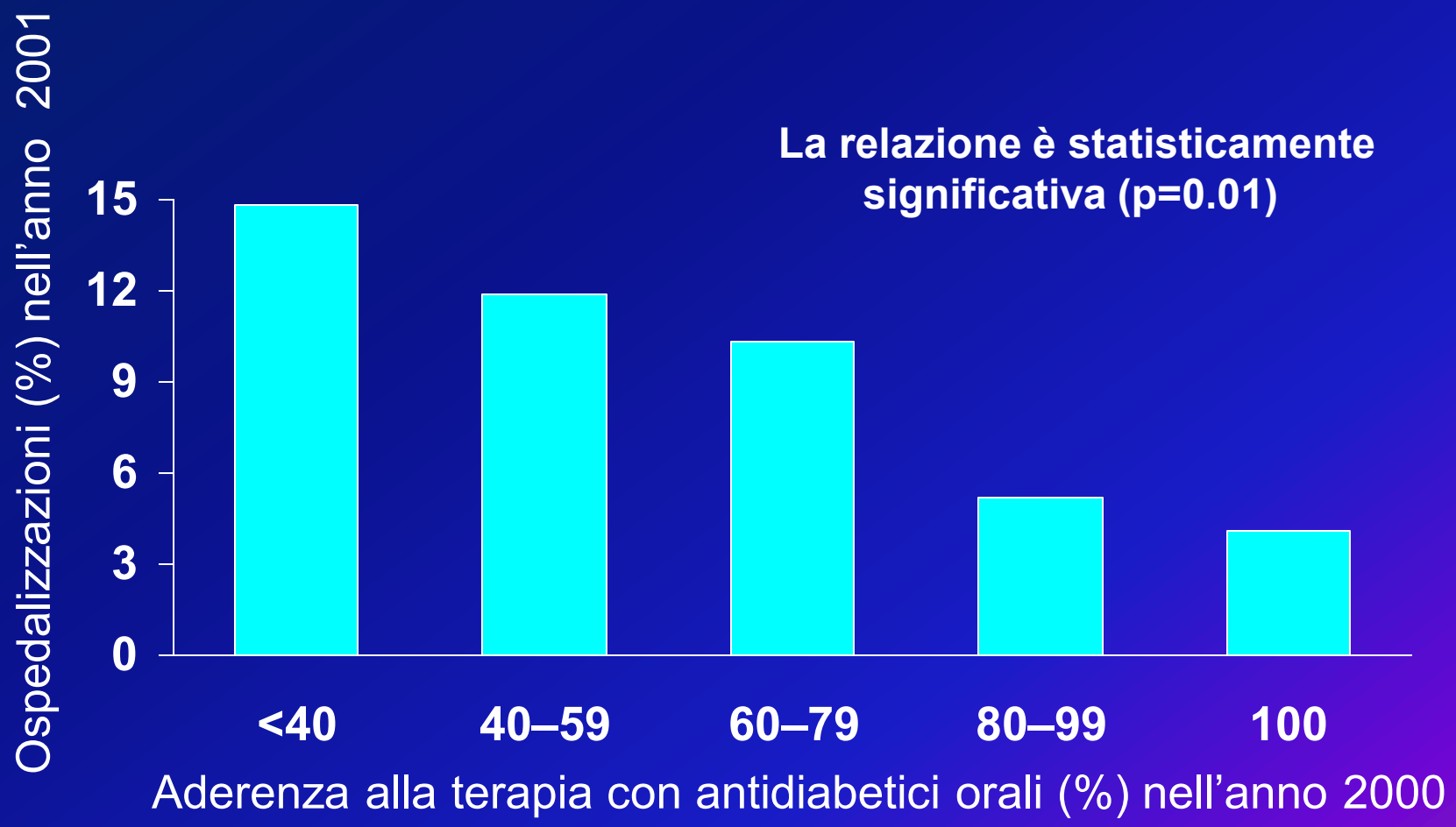
Effetto sulla glicemia



Variazione nel tempo della relazione dose-risposta in termini di glicemia a digiuno, in 75 pazienti trattati per 24 settimane con un dosaggio medio (1500 mg/die) o elevato (3000 mg/die) di metformina; studio clinico randomizzato, controllato, in doppio cieco.

Diabetes Care (1996); 19:64-66

Aderenza e rischio di ospedalizzazione



Lau DT et al. Diabetes Care (2004);27:2149-53.

News

Metformina in polvere verso Metformina in compresse

- Migliora la compliance:
  - Riduce il numero totale di compresse da assumere
  - Evita di confondere la metformina con gli altri farmaci riducendo il rischio di:
    - assumere un farmaco al posto di un altro
    - sottodosaggi o sovradosaggi

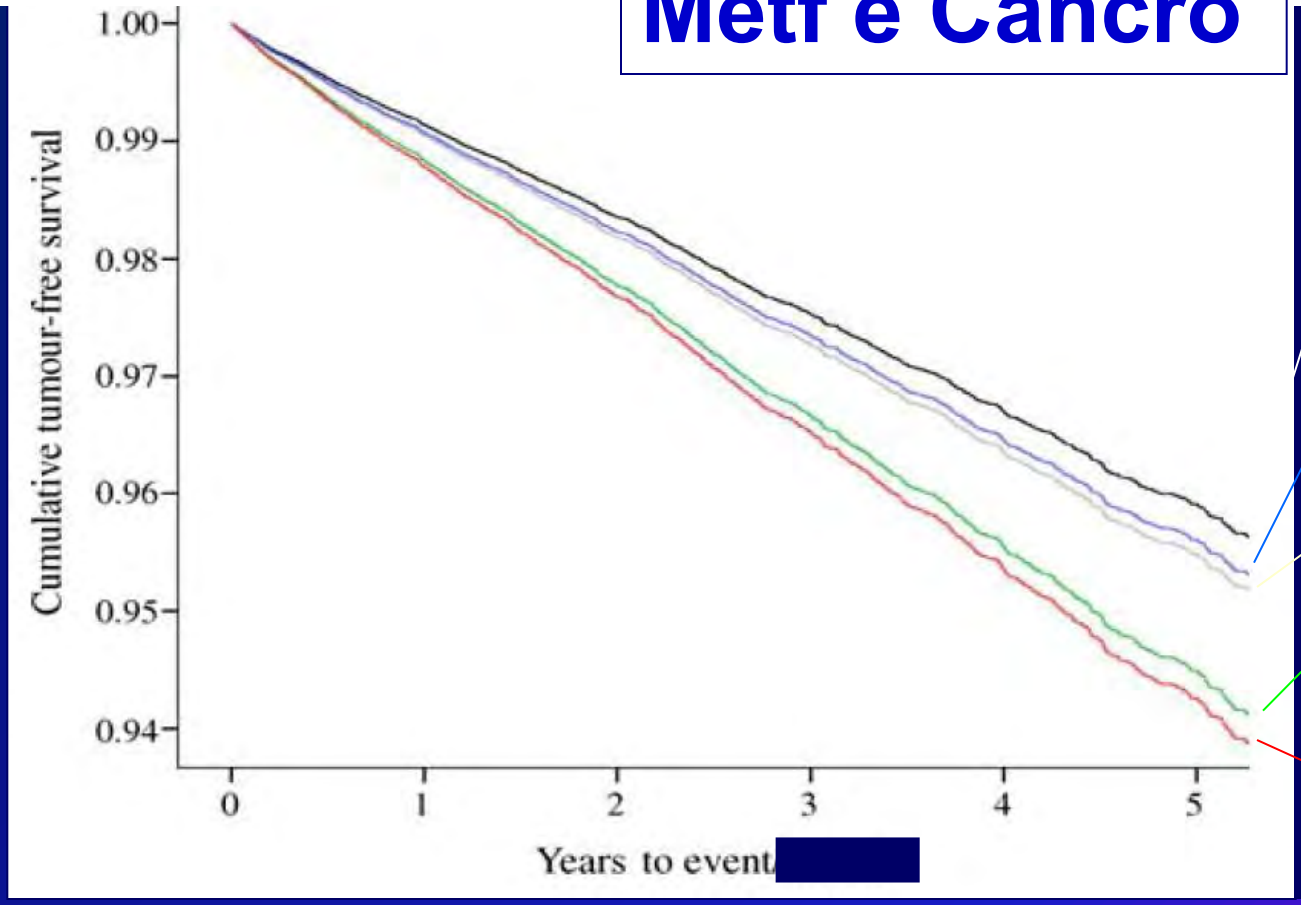
Diabetologia (2009) 52:1766–1777
DOI 10.1007/s00125-009-1440-6

ARTICLE

The influence of glucose-lowering therapies on cancer risk in type 2 diabetes

C. J. Currie · C. D. Poole · E. A. M. Gale

Metf e Cancro



Metformina monot.

Metformina + sulf.

NO DIABETE

Sulfonilurea monot.

Insulina

Sopravvivenza cumulativa libera da tumori solidi in soggetti diabetici e non diabetici, corretta per età, sesso, fumo, condizione sociale e precedente patologia tumorale.

Diabetologia (2009) 52:1766-1777

Metformina e Cancro

Epidemiology/Health Services Research
ORIGINAL ARTICLE

Metformin Associated With Lower Cancer Mortality in Type 2 Diabetes

ZODIAC-16

Gijs W.D. Landman, MD[1,2]
Nanne Kleefstra, MD[2,3]
Kornelis J.J. van Hateren, MD[2]
Klaas H. Groenier, PHD[4]
Rijk O.B. Gans, MD, PHD[5]
Henk J.G. Bilo, MD, PHD, FRCP[2,5]

OBJECTIVE — Several studies have suggested an association between specific diabetes treatment and cancer mortality. We studied the association between metformin use and cancer mortality in a prospectively followed cohort.

RESEARCH DESIGN AND METHODS — In 1998 and 1999, 1,353 patients with type 2 diabetes were enrolled in the Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC) study in the Netherlands. Vital status was assessed in January 2009. Cancer mortality rate was evaluated using standardized mortality ratios (SMRs), and the association between metformin use and cancer mortality was evaluated with a Cox proportional hazards model, taking possible confounders into account.

RESULTS — Median follow-up time was 9.6 years, average age at baseline was 68 years, and average A1C was 7.5%. Of the patients, 570 died, of which 122 died of malignancies. The SMR for cancer mortality was 1.47 (95% CI 1.22–1.76). In patients taking metformin compared with patients not taking metformin at baseline, the adjusted hazard ratio (HR) for cancer mortality was 0.43 (95% CI 0.23–0.80), and the HR with every increase of 1 g of metformin was 0.58 (95% CI 0.36–0.93).

CONCLUSIONS — In general, patients with type 2 diabetes are at increased risk for cancer mortality. In our group, metformin use was associated with lower cancer mortality compared with nonuse of metformin. Although the design cannot provide a conclusion about causality, our results suggest a protective effect of metformin on cancer mortality.

Diabetes Care 33:322–326, 2010

been suggested that hyperinsulinemia promotes carcinogenesis (10). Conversely, metformin may have protective effects on cancer development. Metformin targets AMP-activated protein kinase, which induces glucose uptake in muscles. Activation of AMP-activated protein kinase requires LKB1, a well-known tumor suppressor. The relationship between metformin and LKB1 could therefore be an explanation for the potential beneficial effects of metformin on cancer development (11).

Two previous studies showed tha cancer risk was lower in patients exposed to metformin than in unexposed patients (12,13). Metformin has also been shown to be potentially beneficial in patients with specific types of cancer. For example, type 2 diabetic patients receiving neo adjuvant chemotherapy for breast cance as well as metformin were more likely t have a complete remission than patients not receiving metformin (14). Further more, patients receiving metformin seem to have a lower incidence of prostate and pancreatic cancer (15,16).

Metformin and cancer mortality in type 2 diabetes

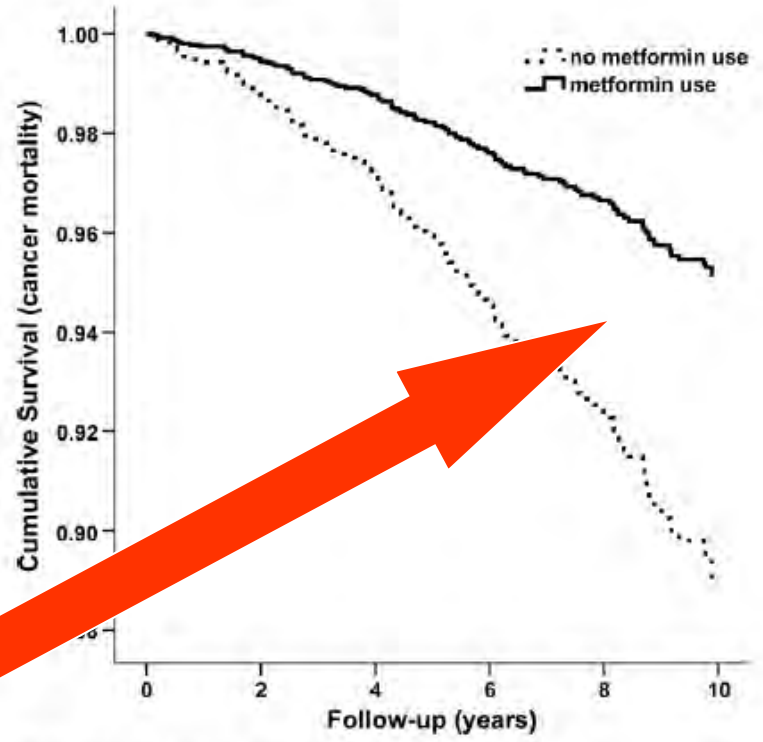


Figure 1—*Cumulative survival curve for cancer mortality.*

1350 paz Diab seguiti per 9,6 a. 570 dec di cui 122 per ADK

Tasso di mort per ADK è di 1,47.

Il gruppo trattato con Metformina ha una mortalità ridotta

METFORMINA

1. Efficace nella prevenzione del DM in soggetti ad alto rischio (DPP)
2. Efficace nel ridurre i livelli di HbA1c (UKPDS)
3. Efficace nel ridurre le complicanze cardiovascolari (IMA)
4. Si associa ad una minore incidenza e mort per Tumori
5. Aggiunta a Insulina :
   riduce il peso corporeo
   riduce il fabbisogno insulinico
   migliora il compenso metabolico

protrarre la terapia con metformina anche

dopo l'inizio della Insulina nel DMT2 se NON controindicata

Gli antidiabetici orali
i farmaci Tradizionali

Insulino-sensibilizzanti

Metformina

Glitazoni

Secretagoghi

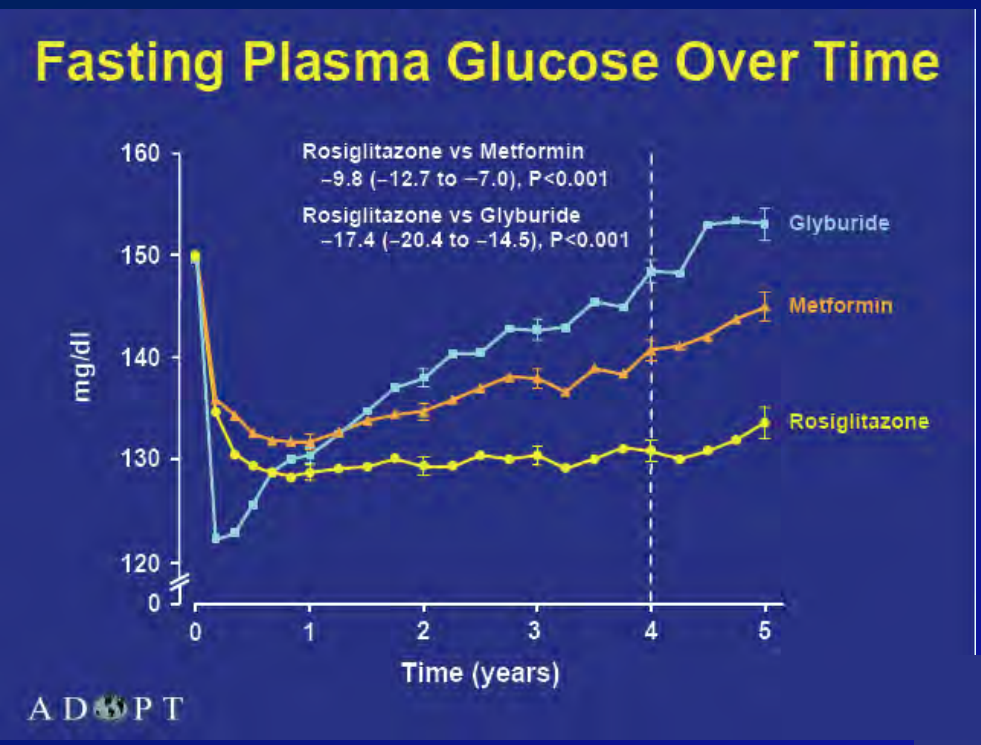
Sulfoniluree

Glinidi

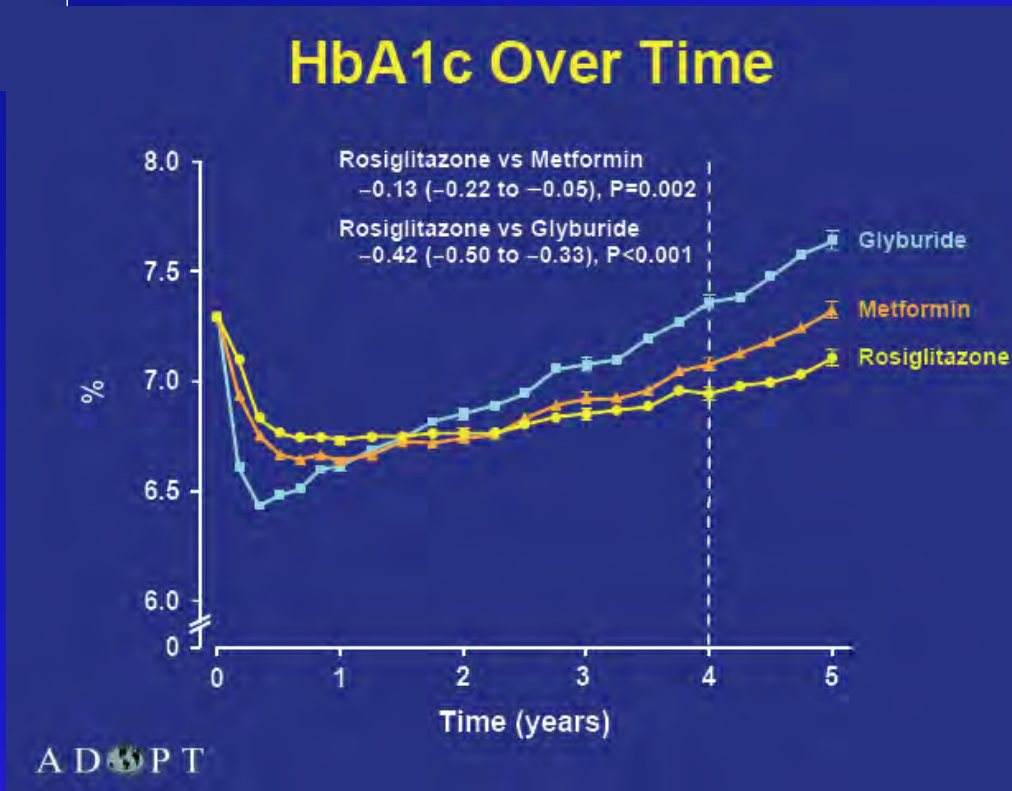
Modificatori dell'assorbimento intestinale

Inibitori dell'α-Glucosidasi intestinale

Lo Studio ADOPT
la durability



a 5 a. fallimento del
15% con Rosi
21% con Metf.
34% con Glib.



GLITAZONI : insulinosensibilizzanti

~~ROSI~~

~~PIO~~ ?

PIO: ritirato in Francia per aumentato rischio di CA vescicale

rischio reale o accanimento terapeutico ?

Gli antidiabetici orali
i farmaci Tradizionali

Insulino-sensibilizzanti

Metformina

Glitazoni

Secretagoghi

Sulfoniluree

Glinidi

Modificatori dell'assorbimento intestinale

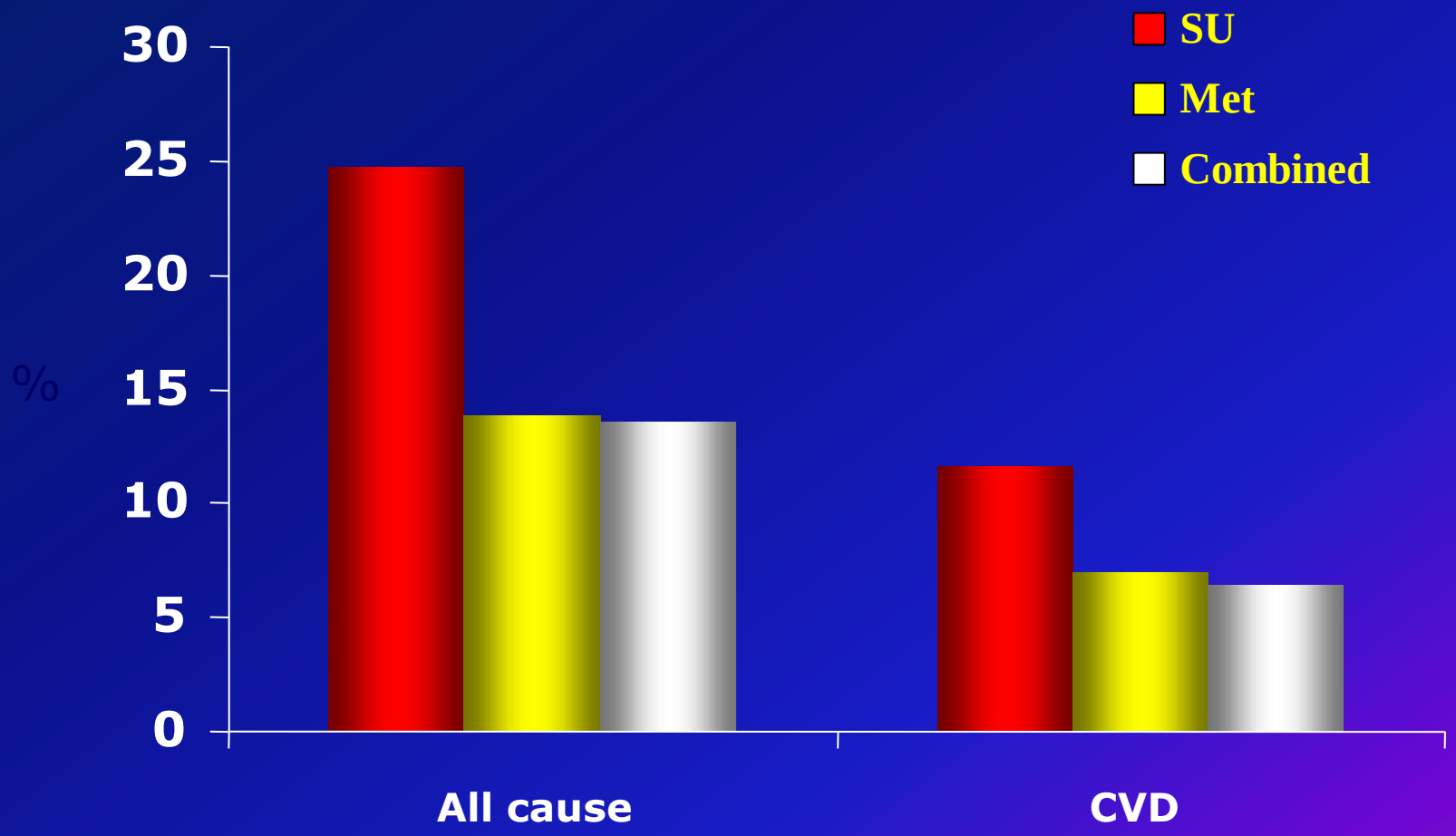
Inibitori dell'α-Glucosidasi intestinale

Sulfoniluree

- tutte le molecole sono in grado di ridurre l'HbA1c di circa 1-1,5% (22,86) e
- sono ancora le più usate in Italia
- Sono disponibili vari studi di confronto solo fra glimepiride e glibenclamide (detta anche gliburide) che tuttavia concludono per una sostanziale pari efficacia
- salvo una minore incidenza di ipoglicemie con gliclazide

Standard Italiani di cura 2010

Decreased Mortality Associated With the Use of Metformin Compared With Sulfonylurea Monotherapy in Type 2 Diabetes



Johnson et al Diabetes Care 25:2244-2248, 2002

European Heart Journal (1999) 20, 439–446
Article No. ehj.1998.1242, available online at http://www.idealibrary.com on IDEAL

Sulfonylureas and ischaemic preconditioning

A double-blind, placebo-controlled evaluation of glimepiride and glibenclamide

H. Klepzig*, G. Kobert†, C. Matter‡, H. Luus§, H. Schneider*, K. H. Boedeker†, W. Kiowski‡, F. W. Amann‡, D. Gruber*, S. Harris§ and W. Burger*

*Department of Medicine, Division of Cardiology, J. W. Goethe University Frankfurt/Main, Germany; †Department of Cardiology, Klinik Nordrhein, Bad Nauheim, Germany; ‡Division of Cardiology, University Hospital, University of Zurich, Zurich, Switzerland; §Division of Runneiry, Farmovs Research Centre for Clinical Pharmacology and Drug Development, University of the Orange Free State, Bloemfontein, South Africa

- ✓ Sulphonylurea : può aumentare la mortalità in paz che debbano fare una PTCA in urgenza o in elezione

- ✓ perciò SOSPENDERE le SU

NO Glibenclamide

Se c'è Card Isch. Cronica

DIABETES/METABOLISM RESEARCH AND REVIEWS
Diabetes Metab Res Rev 2007; **23**: 479–484.
Published online 23 March 2007 in Wiley InterScience (www.interscience.wiley.com) **DOI:** 10.1002/dmrr.736

RESEARCH ARTICLE

Are sulphonylureas all the same? A cohort study on cardiovascular and cancer-related mortality

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A. Barchielli[2]
G. Masotti[1]
E. Buiatti[3]
N. Marchionni[1]
E. Mannucci[1]*

[1]*Geriatric Unit, Department of Critical Care, University of Florence Medical School, Florence, Italy*

[2]*Epidemiology Unit, Local Health Unit 10, Florence, Italy*

[3]*ARSA (Agenzia Regionale Sanità), Florence, Italy*

*Correspondence to: E. Mannucci, Sezione di Diabetologia, Unità Universitaria di Geriatria, Ospedale di Careggi, Via delle Oblate, 4-50141 Firenze, Italy. E-mail: edoardo.mannucci@fastwebnet.it

Abstract

Background Aim of the present study is the comparison of all-cause, cardiovascular and non-cardiovascular mortality, and cardiac morbidity, between patients treated with glibenclamide and gliclazide.

Methods A retrospective observational cohort study was performed on a consecutive series of 568 outpatients (282 women, 286 men) with type 2 diabetes treated with either glibenclamide ($n = 378$) or gliclazide ($n = 190$). Information on all-cause mortality and on causes of death up to 31 December 2004 was obtained by the City of Florence Registry Office. Non-fatal cases requiring hospitalization were identified through the regional hospital discharge system using International Classification of Diseases.

Results Mean follow-up was 5.0 ± 1.6 and 4.4 ± 2.0 years for death and cardiac events, respectively; during follow-up, 33 and 11 deaths were observed in the glibenclamide and gliclazide groups, with a yearly mortality rate of 4.3 and 2.2%, respectively ($p < 0.05$). At Cox regression, after adjustment for potential confounders, including comorbidity, glibenclamide treatment was associated with a significant increase in all-cause mortality [OR 2.1(1.2;2.7), $p < 0.05$], while the difference in cardiovascular mortality was not statistically significant after adjustment for age and sex. Mortality for malignancies was significantly higher in patients treated with glibenclamide after adjustment for age, sex, BMI, and insulin and metformin treatment, [OR 3.6(1.1;11.9); $p < 0.05$]. A higher incidence of cardiac events was associated with glibenclamide treatment only in patients with previously known ischaemic heart disease.

Conclusions Treatment with glibenclamide could be associated with higher mortality for cardiovascular diseases and malignancies, in comparison with gliclazide.

Keywords diabetes mellitus; sulphonylureas; mortality

A higher incidence of cardiac events was associated with glibenclamide treatment only in patients with previously known ischaemic heart disease.

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*

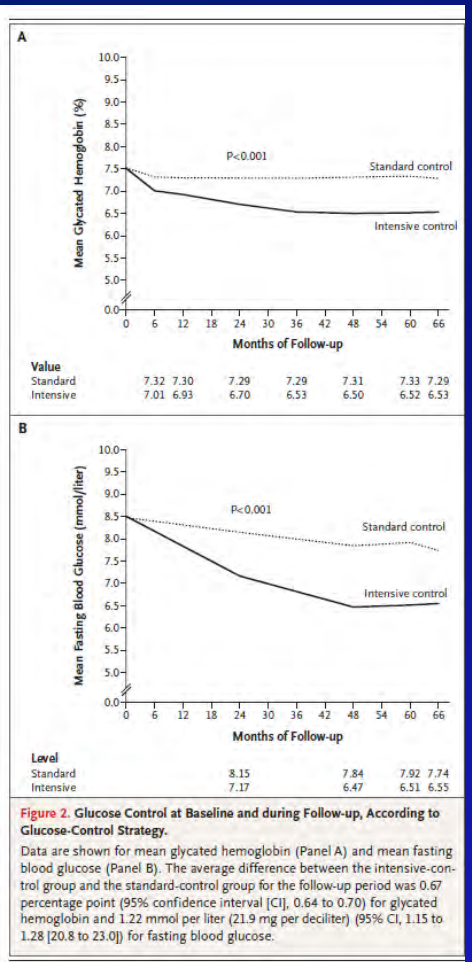


Figure 2. Glucose Control at Baseline and during Follow-up, According to Glucose-Control Strategy.

Data are shown for mean glycated hemoglobin (Panel A) and mean fasting blood glucose (Panel B). The average difference between the intensive-control group and the standard-control group for the follow-up period was 0.67 percentage point (95% confidence interval [CI], 0.64 to 0.70) for glycated hemoglobin and 1.22 mmol per liter (21.9 mg per deciliter) (95% CI, 1.15 to 1.28 [20.8 to 23.0]) for fasting blood glucose.

ADVANCE

N ENGL J MED 358;24

Gliclazide

A rilascio modificato:

< 10% combined outcome

< 21% nefropatia

BACKGROUND

In patients with type 2 diabetes, the effects of intensive glucose control on v outcomes remain uncertain.

METHODS

We randomly assigned 11,140 patients with type 2 diabetes to undergo eith dard glucose control or intensive glucose control, defined as the use of gl (modified release) plus other drugs as required to achieve a glycated hem value of 6.5% or less. Primary end points were composites of major macrov events (death from cardiovascular causes, nonfatal myocardial infarction, or n stroke) and major microvascular events (new or worsening nephropathy or re thy), assessed both jointly and separately.

RESULTS

After a median of 5 years of follow-up, the mean glycated hemoglobin le lower in the intensive-control group (6.5%) than in the standard-control group Intensive control reduced the incidence of combined major macrovascular and vascular events (18.1%, vs. 20.0% with standard control; hazard ratio, 0.9 confidence interval [CI], 0.82 to 0.98; P=0.01), as well as that of major microv events (9.4% vs. 10.9%; hazard ratio, 0.86; 95% CI, 0.77 to 0.97; P=0.01), pr because of a reduction in the incidence of nephropathy (4.1% vs. 5.2%; hazar 0.79; 95% CI, 0.66 to 0.93; P=0.006), with no significant effect on retin (P=0.50). There were no significant effects of the type of glucose control o macrovascular events (hazard ratio with intensive control, 0.94; 95% CI, 0.84 P=0.32), death from cardiovascular causes (hazard ratio with intensive contr 95% CI, 0.74 to 1.04; P=0.12), or death from any cause (hazard ratio with in control, 0.93; 95% CI, 0.83 to 1.06; P=0.28). Severe hypoglycemia, although mon, was more common in the intensive-control group (2.7%, vs. 1.5% standard-control group; hazard ratio, 1.86; 95% CI, 1.42 to 2.40; P<0.001).

CONCLUSIONS

A strategy of intensive glucose control, involving gliclazide (modified relea other drugs as required, that lowered the glycated hemoglobin value to 6.5% a 10% relative reduction in the combined outcome of major macrovascu microvascular events, primarily as a consequence of a 21% relative reduc nephropathy. (ClinicalTrials.gov number, NCT00145925.)

Sicurezza a lungo termine della monoterapia con sulfoniluree

- analisi nazionale danese sulla popolazione residente d'età >20 anni che aveva iniziato una monoterapia con una SU o METF nel periodo 1997 e il 2006,
- valutandone (attraverso un follow-up della durata massima di 9 anni) il rischio di mortalità complessiva, di quella CV e degli eventi ischemici miocardici e cerebrali non fatali
- **107.806 soggetti, 9607 con IMA:**
- Rispetto a **Metformina,** l'assunzione di

  glimepiride (hazard ratio [HR] 1,32; IC 95% 1,24-1,40),

  glibenclamide (HR 1,19; IC 95% 1,11-1,28),

  glipizide (HR 1,27; IC 95% 1,17-1,38) e

è risultata associata a un aumento del rischio di mortalità per tutte le cause, nei pazienti senza precedenti eventi coro, e con pregresso IMA

- **NO per gliclazide e per repaglinide**

Tina Ken Schramm .Eur Heart J. 2011 Apr 6.

Gli antidiabetici orali
i farmaci Tradizionali

Insulino-sensibilizzanti

Metformina

Glitazoni

Secretagoghi

Sulfoniluree

Glinidi

Modificatori dell'assorbimento intestinale

Inibitori dell'α-Glucosidasi intestinale

Acarbose :

- Inibitori dell'a-Glucosidasi intestinale
- Rallenta l'assorbimento del glucosio legandosi al medesimo recettore
- Riduce l' iperglicemia post-prandiale e non da ipoglicemie
- Utile in Prevenzione 1aria (STOP)

Effetti Collaterali gastro-intestinali

Ridotti nettamente dalla titolazione graduale

- Oggi a carico del SSN
- Basso costo

Epidemiology/Health Services/Psychosocial Research
ORIGINAL ARTICLE

Increased Cancer-Related Mortality for Patients With Type 2 Diabetes Who Use Sulfonylureas or Insulin

SAMANTHA L. BOWKER, MSC[1,2]
SUMIT R. MAJUMDAR, MD, MPH[1,3]
PAUL VEUGELERS, PHD[2]
JEFFREY A. JOHNSON, PHD[1,2]

	Total *n*	Cancer deaths	Cancer mortality rate (per 1,000 person-years) (%)	Adjusted HR (95% CI)*
Oral antidiabetics				
Metformin	6,969	245 (3.5)	6.3	1.0†
Sulfonylurea	3,340	162 (4.9)	9.7	1.3 (1.1–1.6)
Insulin use				
No insulin use	8,866	323 (3.6)	6.8	1.0†
Insulin use	1,443	84 (5.8)	9.9	1.9 (1.5–2.4)
Age (years)				
≤53.9	2,578	16 (0.6)	1.1	1.0†
54.0–64.3	2,578	75 (2.9)	6.0	5.0 (2.9–8.6)
64.4–73.3	2,576	127 (4.9)	8.9	8.9 (5.3–15.0)
≥73.4	2,577	189 (7.3)	15.6	16.9 (10.0–28.3)

10-y NNH (SU vs Met): 35

Diabetes Care 29:254–258, 2006

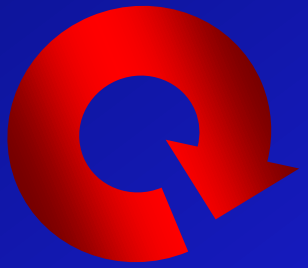
Mind the gap !

Insieme ad i nuovi farmaci, possiamo usare i farmaci tradizionali per confezionare un vestito su misura al paziente DT2

per colmare il Gap

tra goal standard e pratica clinica quotidiana

efficacia teorica



efficacia pratica


AMD
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