



e progressione della malattia renale
nel diabete tipo 2

ARMI A DISPOSIZIONE SINO ALL'AVVENTO DEI NUOVI FARMACI

Marco FIORENTINO

Azienda Ospedaliero Universitaria Policlinico di Bari

*Dipartimento dell'Emergenza e Trapianti d'Organo
Sezione di Nefrologia, Dialisi e Trapianto
Università degli Studi di Bari*



preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

Natural history of type 2 diabetic nephropathy

Management del paziente diabetico con Nefropatia

❖ Diagnosi appropriata (biopsia renale)

❖ Terapia



Quale tra le seguenti non è una indicazione assoluta alla biopsia renale nel paziente diabetico

- a) recente insorgenza di proteinuria nefrosica
- b) rapido peggioramento della funzione renale
- c) proteinuria nefrosica in paziente con breve durata della malattia diabetica
- d) microalbuminuria in paziente con diabete mellito >10 anni con retinopatia diabetica

Diapositiva preparata da MARCO FLORENTINO e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it



Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd



forms of DN are rather developing non-typical features of DN overlap with other

(2017) 32: 97–110

tion 4 May 2016

REVIEW

Indications for renal biopsy in patients with diabetes. Joint position statement of the Italian Society of Nephrology and the Italian Diabetes Society

Salvatore Di Paolo ^{a,*}, Marco Fiorentino ^a, Luca De Nicola ^b, Gianpaolo Reboldi ^c, Loreto Gesualdo ^{d,e}, Federica Barutta ^f, Andrea Natali ^{g,h}, Giuseppe Penno ^{g,i}, Paola Fioretto ^{j,k}, Giuseppe Pugliese ^{l,m} on behalf of the Italian Society of Nephrology and the Italian Diabetes Society

glomerular changes (class 2), other glomerulonephritides superimposed on diabetic glomerulosclerosis (class 3a), or glomerulonephritides without the presence of diabetic glomerulosclerosis (class 3b). Although no significant differences were found for class 2 (detected in 15% and 16% of patients from CRPs and the CUP, respectively), the frequency of the other two classes was strongly biased by the biopsy policy. Class 1 was found in 29% and 51% of cases, and class 3 in 57% and 33% of cases from CRPs and the CUP, respectively. Moreover, class 3a was more common (67%) in the CUP, and class 3b (78%) in CRPs. Our findings may explain conflicting data from the literature and the influence that type of adopted biopsy policy may have on an epidemiological evaluation. This study helps clarify the frequency of renal changes in patients with type 2 diabetes and suggests more extensive use of renal biopsy to obtain reliable prognostic indications and plan a rational therapeutic approach.

© 2002 by the National Kidney Foundation, Inc.



^a1, Davide Bolignano^a, Vladimir Tesar⁴, Anna Pisano², Wim Van Biesen³, ^b1, Graziella D'Arrigo² and Loreto Gesualdo¹ on behalf of the ERA-EDTA ^c1, ^d1, ^e1, ^f1, ^g1, ^h1, ⁱ1, ^j1, ^k1, ^l1, ^m1

Table 1 Indications for renal biopsy in patients with diabetes.

Diagnostic definition in all patients with clinical suspicion of NDRD for the presence of one or more of the following features:

- Diabetic disease duration <5 years (in type 1 diabetes);
- Absence of diabetic retinopathy (particularly in type 1 diabetes);
- Rapid onset and progression of albuminuria or sudden onset of nephrotic syndrome;
- Rapid decline of renal function (GFR) with or without albuminuria;
- Presence of hematuria (dysmorphic erythrocytes);
- Active urine sediment;
- Clinical suspicion of other nephropathies (e.g., vasculitis, amyloidosis);
- Positivity for markers of other systemic diseases (e.g., ANCA, ANA, dsDNA, low complement factors, cryoglobulinemia).

Prognostic evaluation in selected patients with clinical suspicion of DN.

dies on NDRD e values y meta-planning ored by

lence of %, 3 to ely. IgA PVs for ifidence d 19.7% nbining). Meta-luration NDRD, ms and RD and 95% CI:

with dia- ses and ification

according to individual factors is needed for selecting patients who might benefit from biopsy.

Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia. Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

Terapia della Nefropatia Diabetica

- ❖ ***Compenso glicemico***
- ❖ ***Normalizzazione Pressione arteriosa***
- ❖ ***Riduzione della Proteinuria***

Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

Effect of intensive glucose lowering treatment on renal events

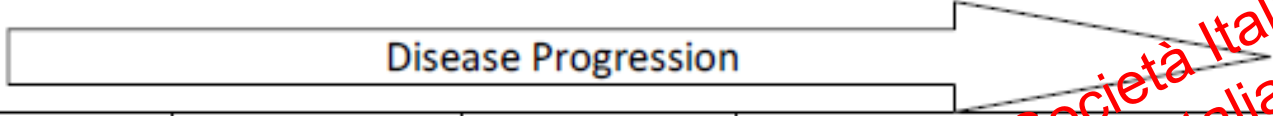
	ACCORD	ADVANCE	UKPDS	VADT	overall ^o
HbA1c	-1,01	-0,72	-0,66	-1,16	-0,88
eventi microvascolari maggiori	0,95	0,86	0,75	-	-
eventi renali*	-	0,79	-	0,62	-
incidenza di microalbuminuria	0,79/0,85	0,91	0,67	0,71	0,90 (0,85-0,96)
incidenza di macroalbuminuria	0,68/0,71	0,7	0,66	0,64	-
raddoppio dei livelli di creatinina	1,07/1,04	1,15	0,26	1	1,03 (0,98-1,08)
ESRD	0,95/0,92	0,64	0,73	0,63	

* nuova nefropatia o progressione della nefropatia.

^o Boussageon 2011.

Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

Intensive glucose control and Outcomes

	UKPDS (n = 3,867)	ADVANCE (n = 11,140)	ACCORD (n = 10,251)	VADT (n = 1,791)
				
Duration of diabetes (yr)	0	8	10	11.5
Mean baseline HbA1c (%)	7.1	7.5	8.3	9.4
Mean baseline FPG (mmol/l)	8.0	8.5	9.7	11.4
Mean age (yr)	53	66	62	60
Micro	↓	↓	=↓	=
Macro	↓	=	↑	=

Compared with UKPDS, which enrolled newly diagnosed patients, recent trials have enrolled high-risk patient populations: longer duration of disease, older age, and more severe hyperglycemia

Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

Effects of Intensive Control of Glycemia on Clinical Kidney Outcomes in Type 2 Diabetes Patients Compared with Standard Control: A Meta-Analysis

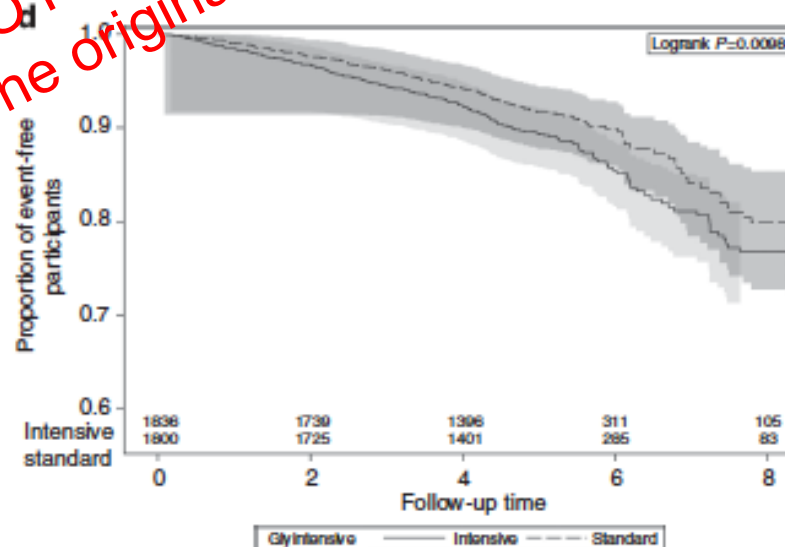
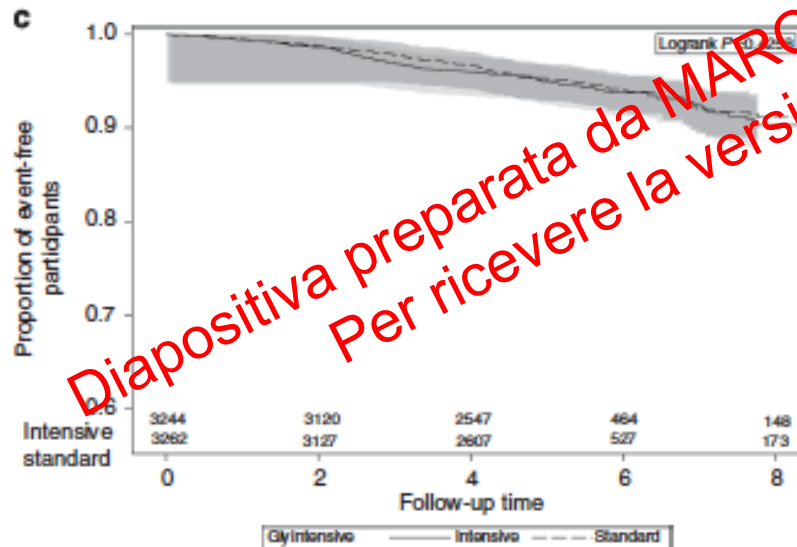
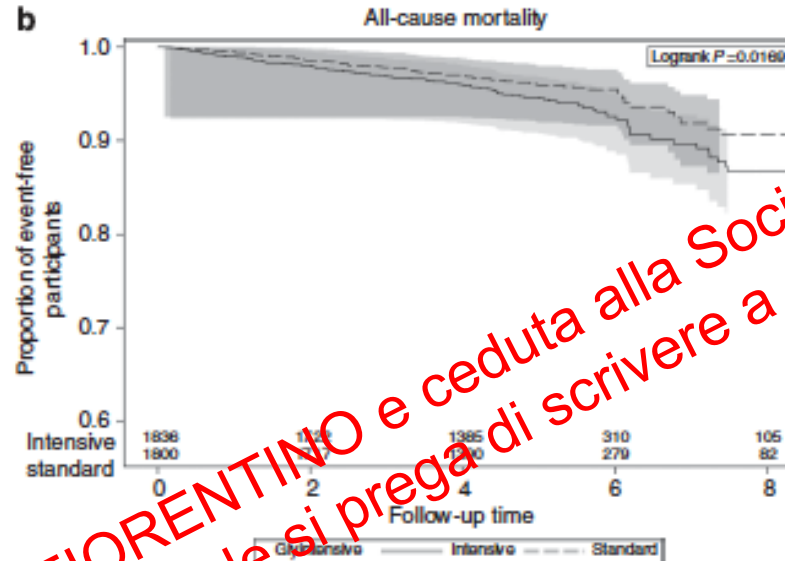
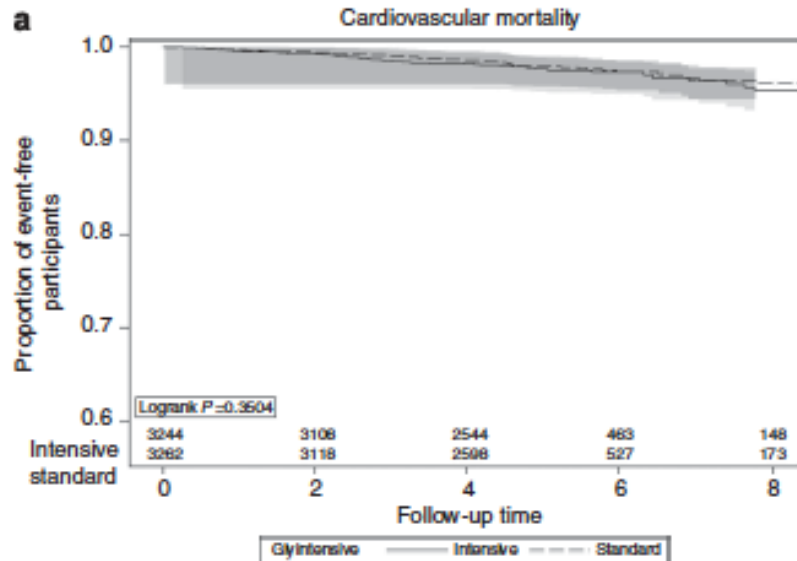


frontiers

in Pharmacology

- ❖ Gli studi disponibili concordano nel riconoscere un effetto dei trattamenti farmacologici sulla albuminuria, mentre è assai dubbio l'impatto favorevole sulla CKD clinicamente manifesta
- ❖ Il controllo glicemico intensivo sembra ridurre solo la mortalità da uremia terminale
- ❖ Probabilmente, la progressione da CKD a ESRD è indipendente dal controllo glicemico, una volta che si sia instaurato il danno d'organo.
- ❖ Inoltre, al progredire della CKD il trattamento intensivo si associa ad incremento di rischio di Ipoglicemia

Intensive glucose control, CKD and CV Outcomes



In high-risk patients with type II diabetes, mild and moderate CKD is associated with increased cardiovascular risk.

Intensive glycemic control significantly increases the risk of cardiovascular and all-cause mortality in this population.

*Papademetriou V, Kidney Int 2015
(ACCORD Study Group)*

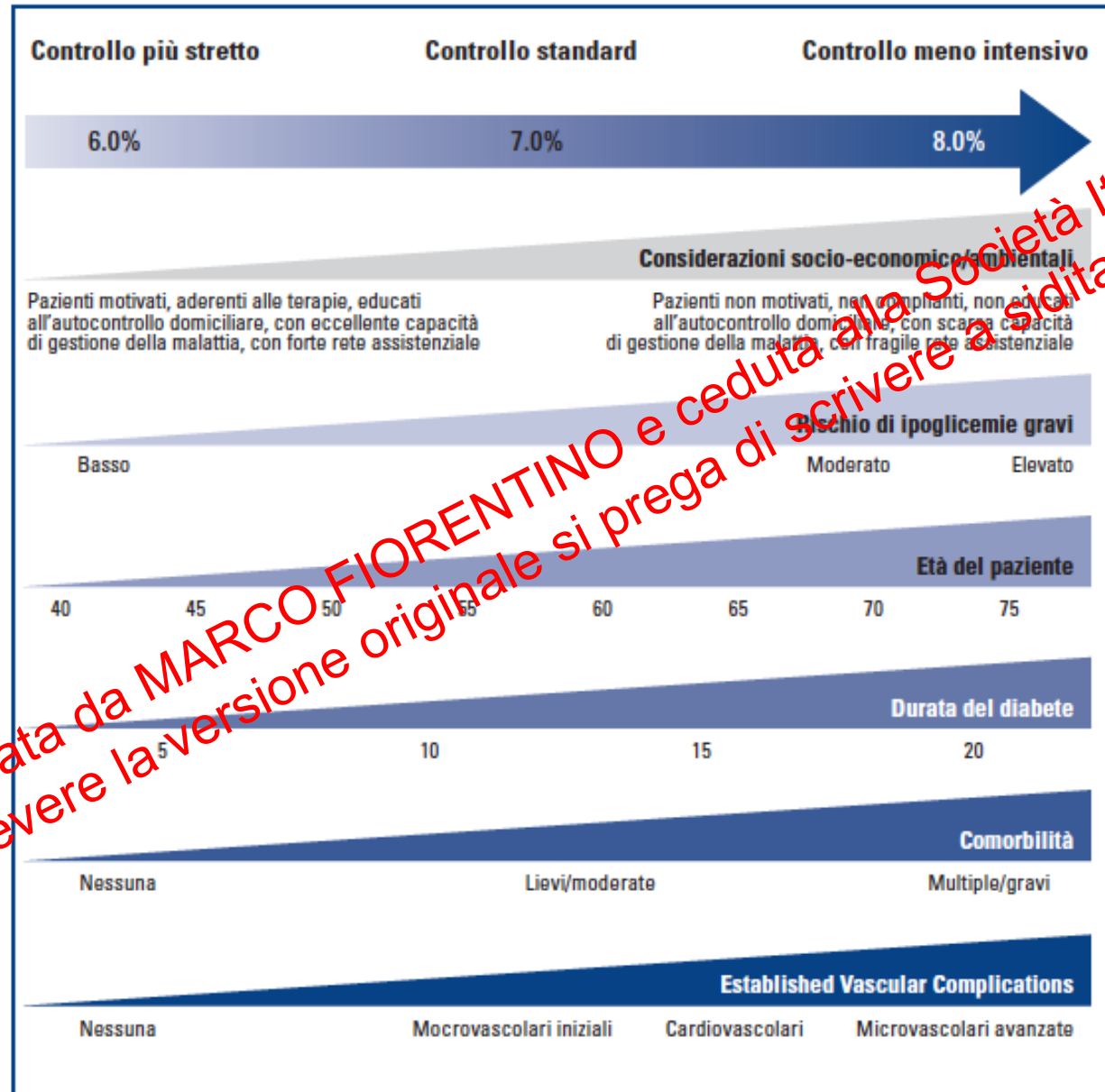
ACCORD, ADVANCE, and VADT Trials were unable to show a significant impact of glycemic control on CV events. These trials included patients with a long duration of the disease, and with previous unsatisfactory glycemic control. Chronic exposure to hyperglycemia may cause a kind of negative metabolic memory, and thereby reduce the potential impact of good glycemic control.

The UKPDS which recruited only subjects with newly diagnosed diabetes and without prior CV events. In these patients, early achievement of glycemic control translated into a long-term reduction of the risk of micro- and macrovascular complications.

This observation supports the need for early and appropriate treatment of hyperglycemia and associated metabolic disturbances (positive “glycemic legacy”).

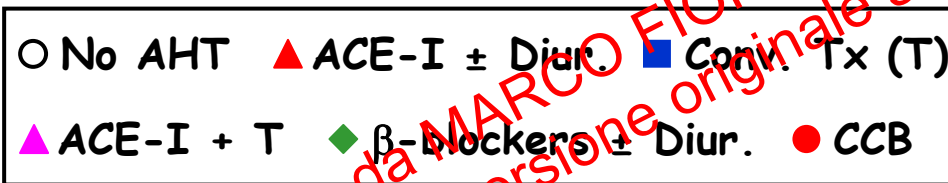
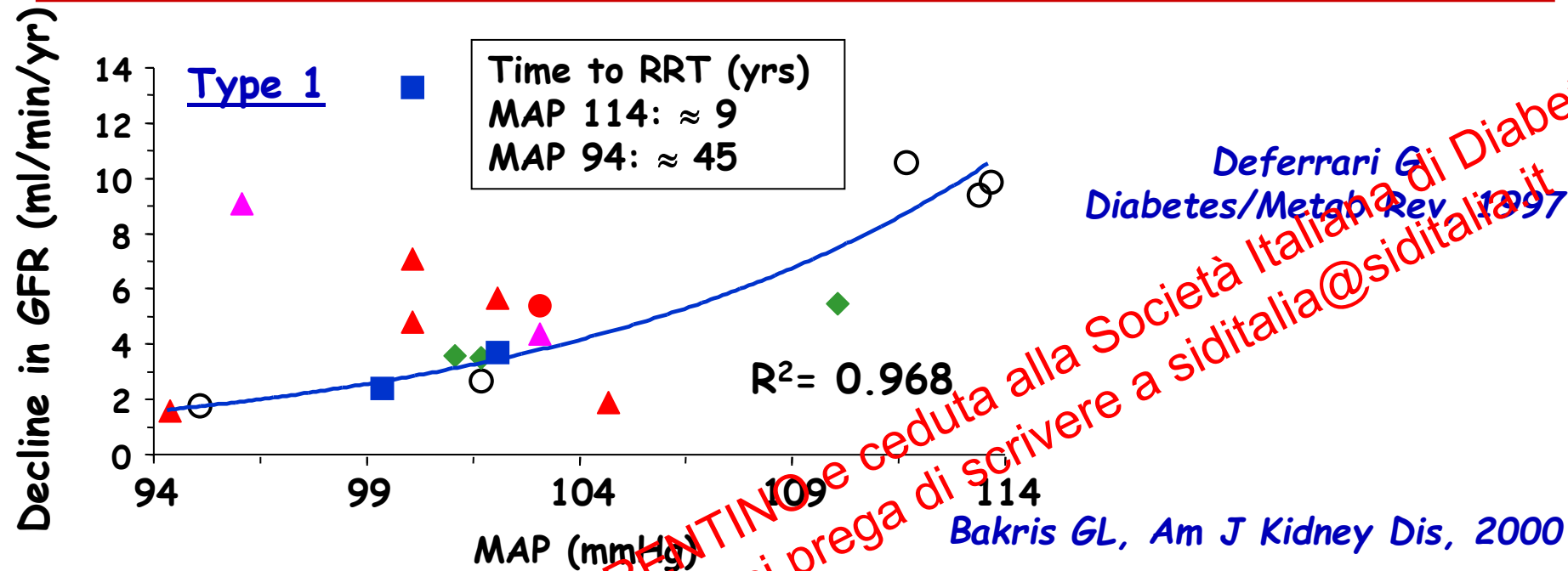
This should be feasible now through the selection of individual targets and personalized pharmacologic treatments. In doing so, the potential risks of intensive treatment might then be avoided.

Treatment goal Personalization

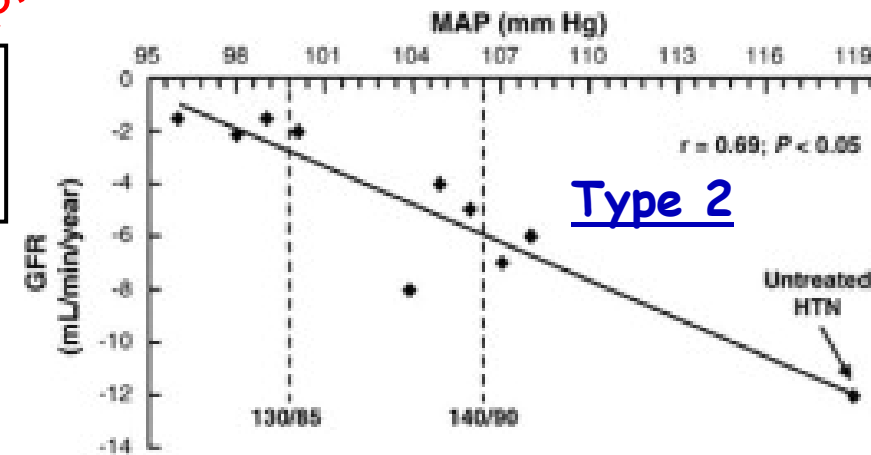


Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

CONTROLLO PRESSORIO: Prevenzione Terziaria



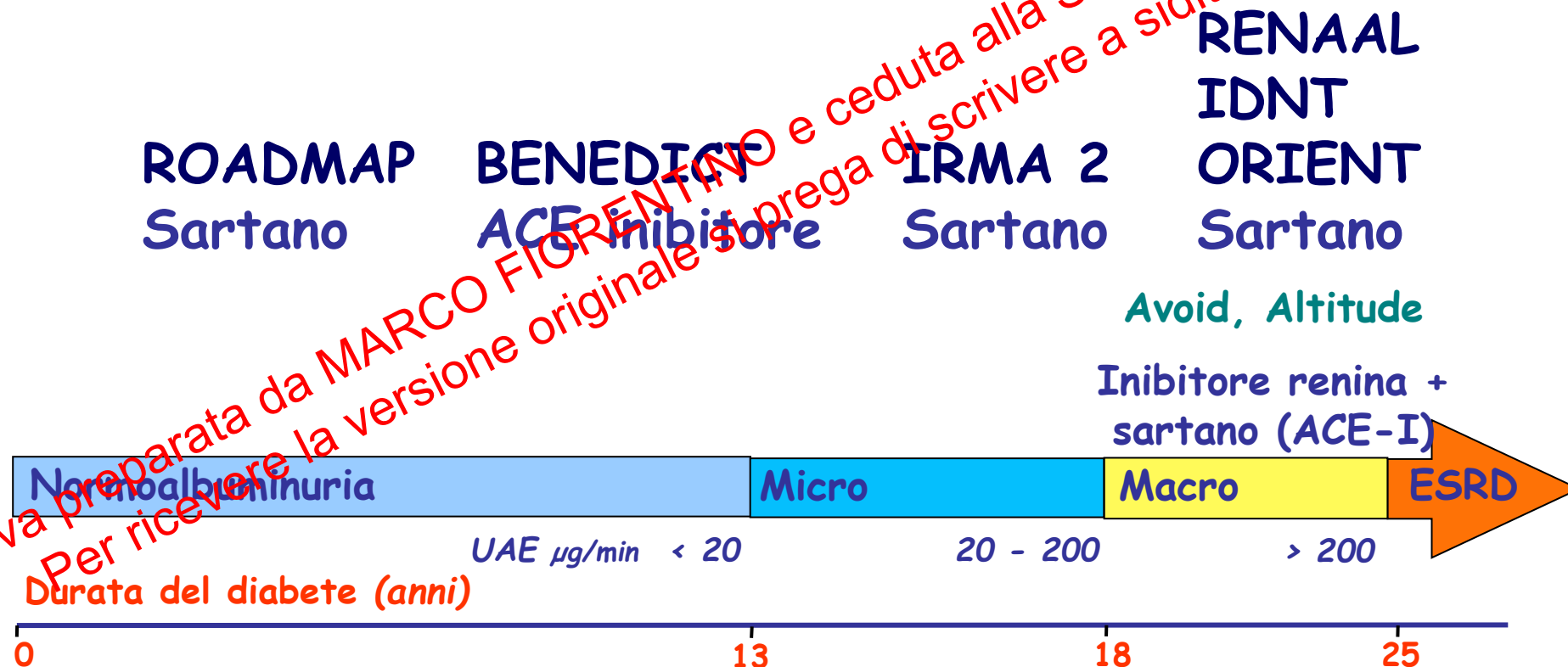
Il controllo pressorio, indipendentemente dalla classe di farmaci utilizzati, rallenta il declino del filtrato glomerulare (PREVENZIONE TERZIARIA) e, forse, la progressione da Micro- a Macro-Albuminuria (PREVENZ.SECONDARIA)



Summary of studies on nephropathy progression used in figure

• Parving HH et al. Br Med J, 1989	• Moschisio G et al. N Engl J Med, 1996*
• Viberti GC et al. JAMA, 1993	• Bakris GL et al. Kidney Int, 1996
• Klor S et al. N Eng J Med, 1993*	• Bakris GL. Hypertension, 1997
• Hebert L et al. Kidney Int, 1994	• GISEN Group, Lancet, 1997*
• Lebovitz H et al. Kidney Int, 1994	

Gli inibitori del Sistema Renina Angiotensina impiegati nelle varie fasi della nefropatia diabetica



Preventing Microalbuminuria in Type 2 Diabetes

Piero Ruggenenti, M.D., Anna Fassi, M.D., Anelja Parvanova Ilieva, M.D., Simona Bruno, M.D., Ilian Petrov Iliev, M.D., Varusca Brusegan, M.D., Nadia Rubis, R.N., Giulia Gherardi, R.N., Federica Arnoldi, R.N., Maria Ganeva, Stat.Sci.D., Bogdan Ene-Iordache, Eng.D., Flavio Gaspari, Ph.D., et al., for the Bergamo Nephrologic Diabetes Complications Trial (BENEDICT) Investigators

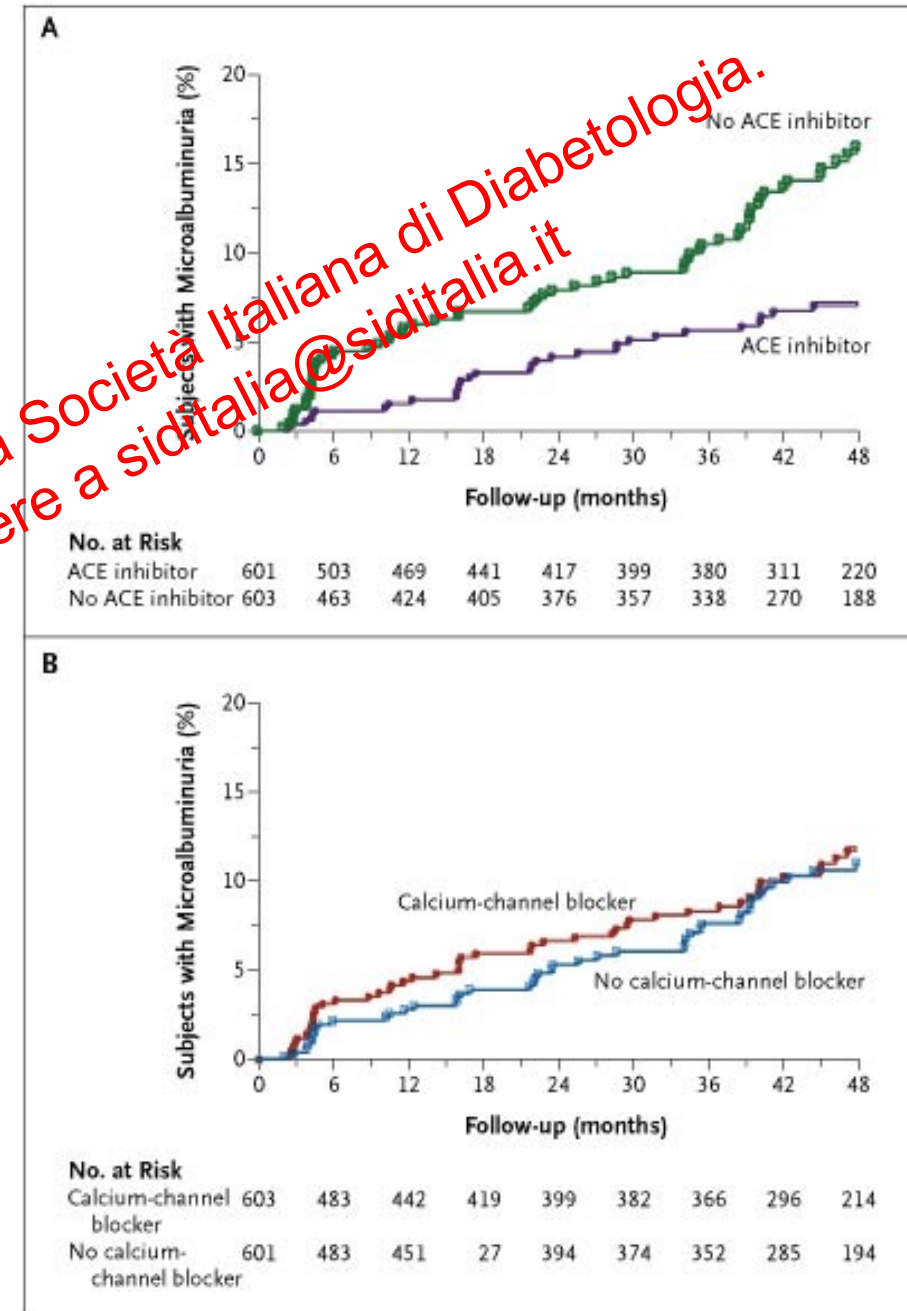
1204 subjects

randomly assigned to receive at least three years of treatment with

- trandolapril (at a dose of 2 mg per day) plus verapamil (sustained-release formulation, 180 mg per day),
- trandolapril alone (2 mg per day),
- verapamil alone (sustained-release formulation, 240 mg per day),
- placebo.

The target blood pressure was 130/80 mm Hg.

The primary end point was the development of persistent microalbuminuria (overnight albumin excretion, ≥ 20 μ g per minute at two consecutive visits).

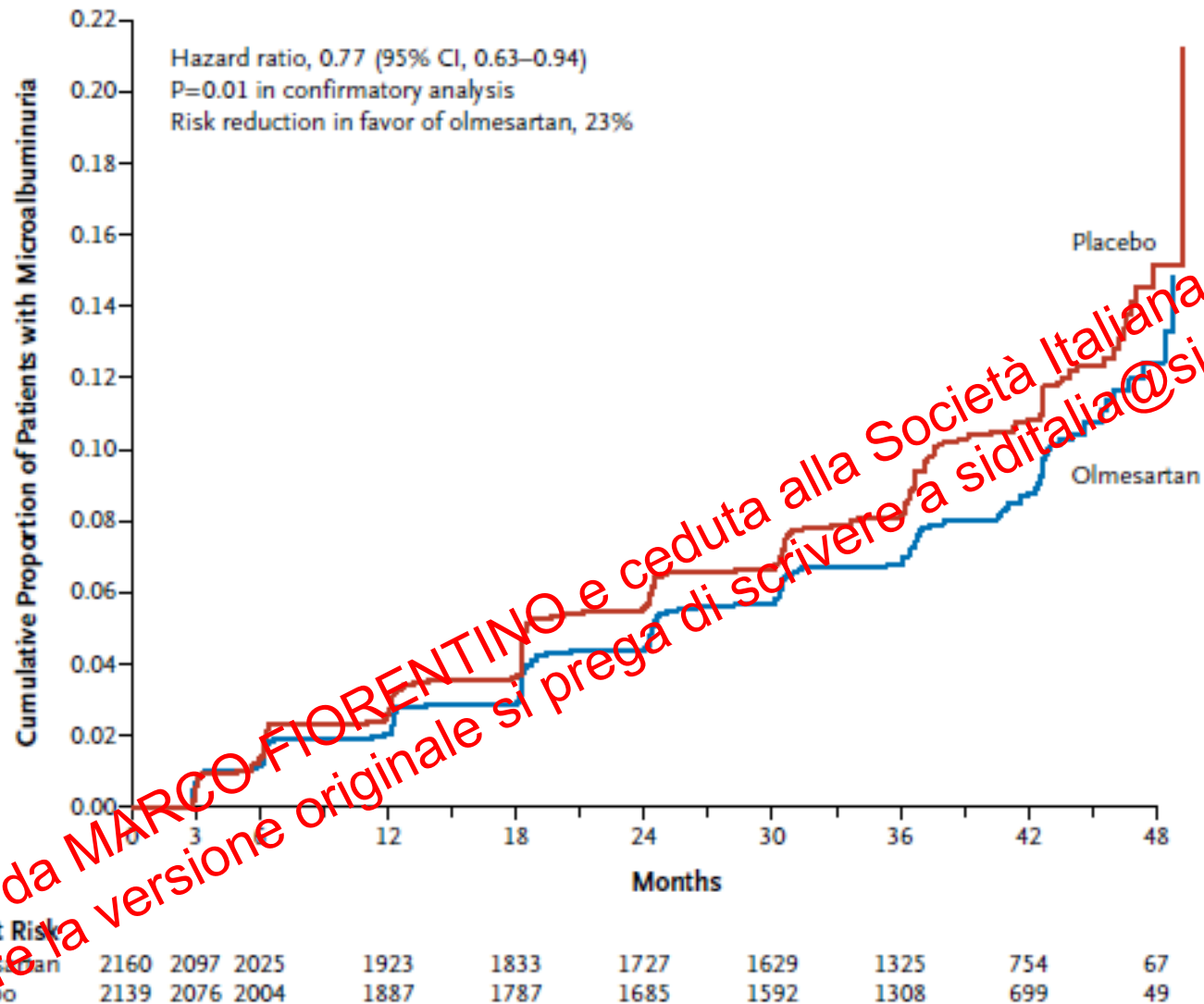


ORIGINAL ARTICLE

Olmesartan for the Delay or Prevention of Microalbuminuria in Type 2 Diabetes

Hermann Haller, M.D., Sadayoshi Ito, M.D., Ph.D., Joseph C. Izzo, Jr., M.D., Andrzej Januszewicz, M.D., Shigehiro Katayama, M.D., Ph.D., Jan Menne, M.D., Albert Mimran, M.D., Ton J. Rabelink, M.D., Ph.D., Eberhard Ritz, M.D., Luis M. Ruilope, M.D., Lars C. Rump, M.D., and Giancarlo Viberti, M.D., for the ABOARDMAP Trial Investigators*

- ❑ Randomized, double-blind trial.
- ❑ 4447 Normoalbuminuric T2DM patients, eGFR: 84.9 ± 17.2 mL/min/1.73 m²
- ❑ Olmesartan 40 mg once daily or placebo for a median of 3.2 years.
- ❑ Target blood pressure less than 130/80 mm Hg.
- ❑ Primary outcome was the time to the first onset of microalbuminuria.



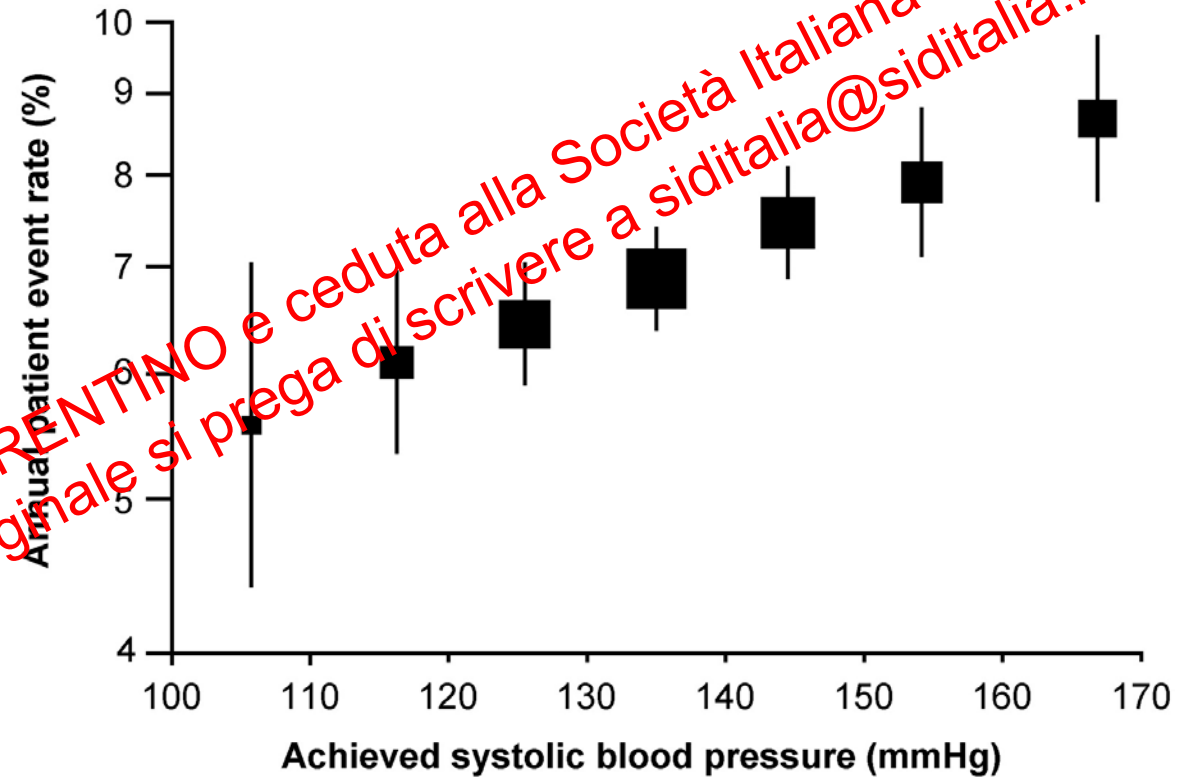
Olmesartan was associated with a delayed onset of microalbuminuria. The higher rate of fatal cardiovascular events with olmesartan among patients with preexisting coronary heart disease is of concern

Lowering Blood Pressure Reduces Renal Events in Type 2 Diabetes *ADVANCE Study*

11.140 pts eGFR<60 ml/min 19% MacroAlbum. 3.5%

Patients were randomly assigned to fixed combination perindopril-indapamide or placebo

During a mean follow-up of 4.3 yr, active treatment reduced the risk for renal events by 21% ($P < 0.0001$), which was driven by reduced risks for developing microalbuminuria and macroalbuminuria (both $P < 0.003$).

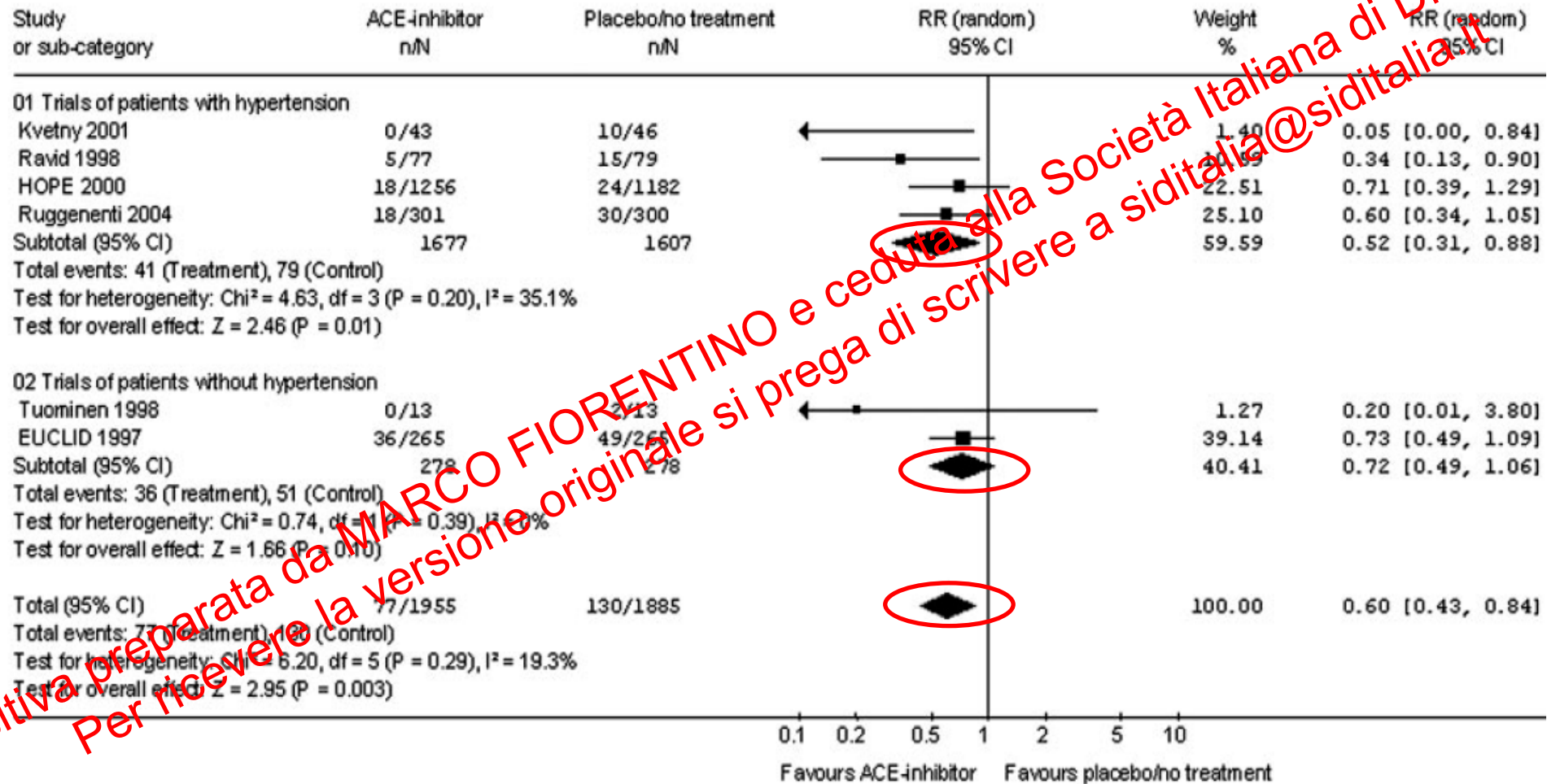


Median systolic blood pressure (mmHg)	106	116	125	135	144	154	168
No. of person-years	1431	4266	8974	11983	9138	4942	3470

Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia. Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

Antihypertensive Agents for Primary Prevention of Diabetic Nephropathy

Giovanni F.M. Strippoli, Maria Craig, Francesco P. Schena, and Jonathan C. Craig

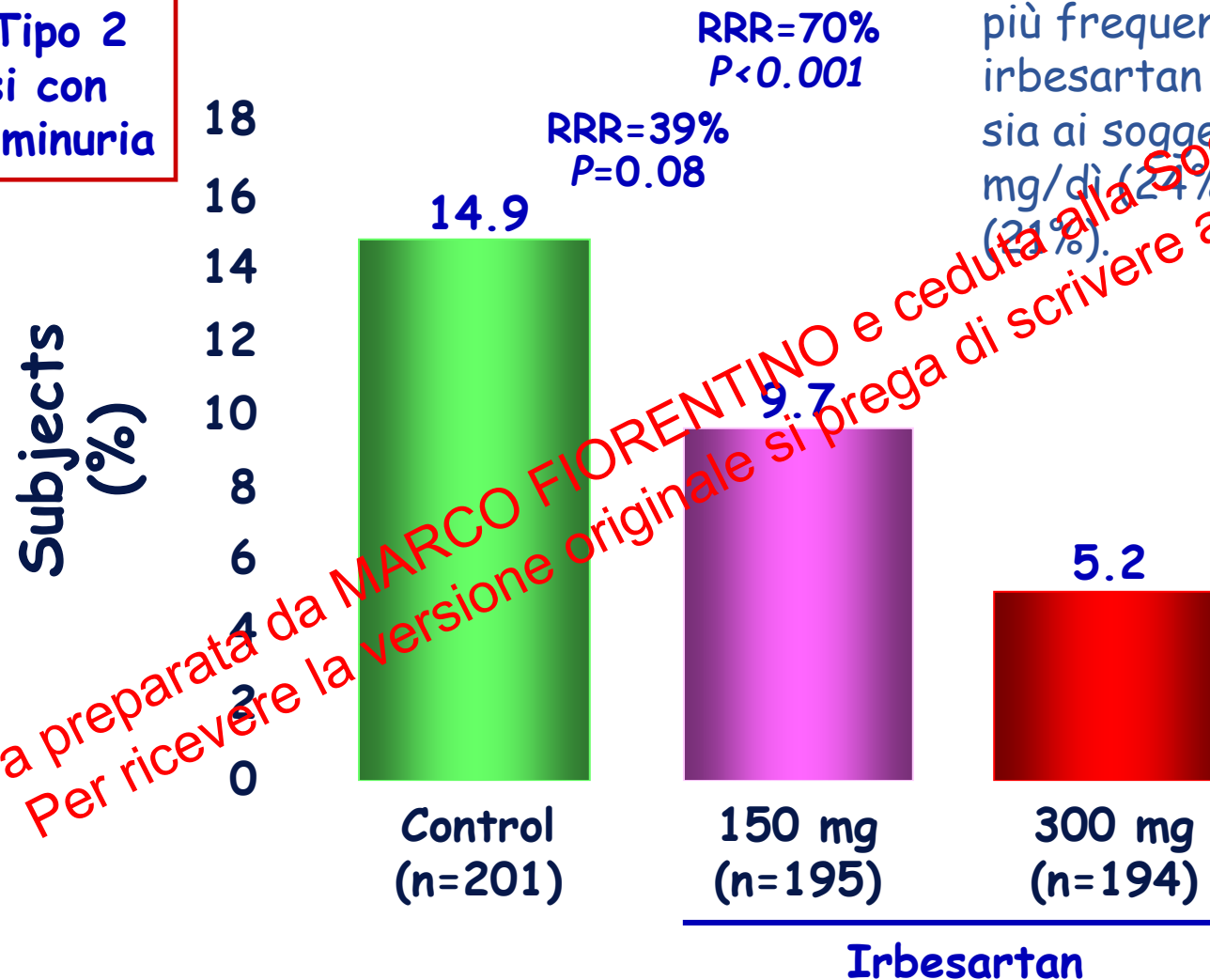


**ACEi e sviluppo di micro-/macro-alb in diabetici normoalb,
sia NORMOTESI che ipertesi**

SARTANI: Prevenzione Secondaria

Studio IRMA 2

590 pz Tipo 2
Ipertesi con
Microalbuminuria



La regressione verso la normoalbuminuria era più frequente nel gruppo in trattamento con irbesartan 300 mg/di (36%; $p=0,006$) rispetto sia ai soggetti trattati con irbesartan 150 mg/di (24%) sia a quelli trattati con placebo (21%).

Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia. Per ricevere la versione originale si prega di scrivere a siiditalia@siiditalia.it

Lowering Blood Pressure Reduces Renal Events in Type 2 Diabetes

Table 4. Incidence of renal end points^a

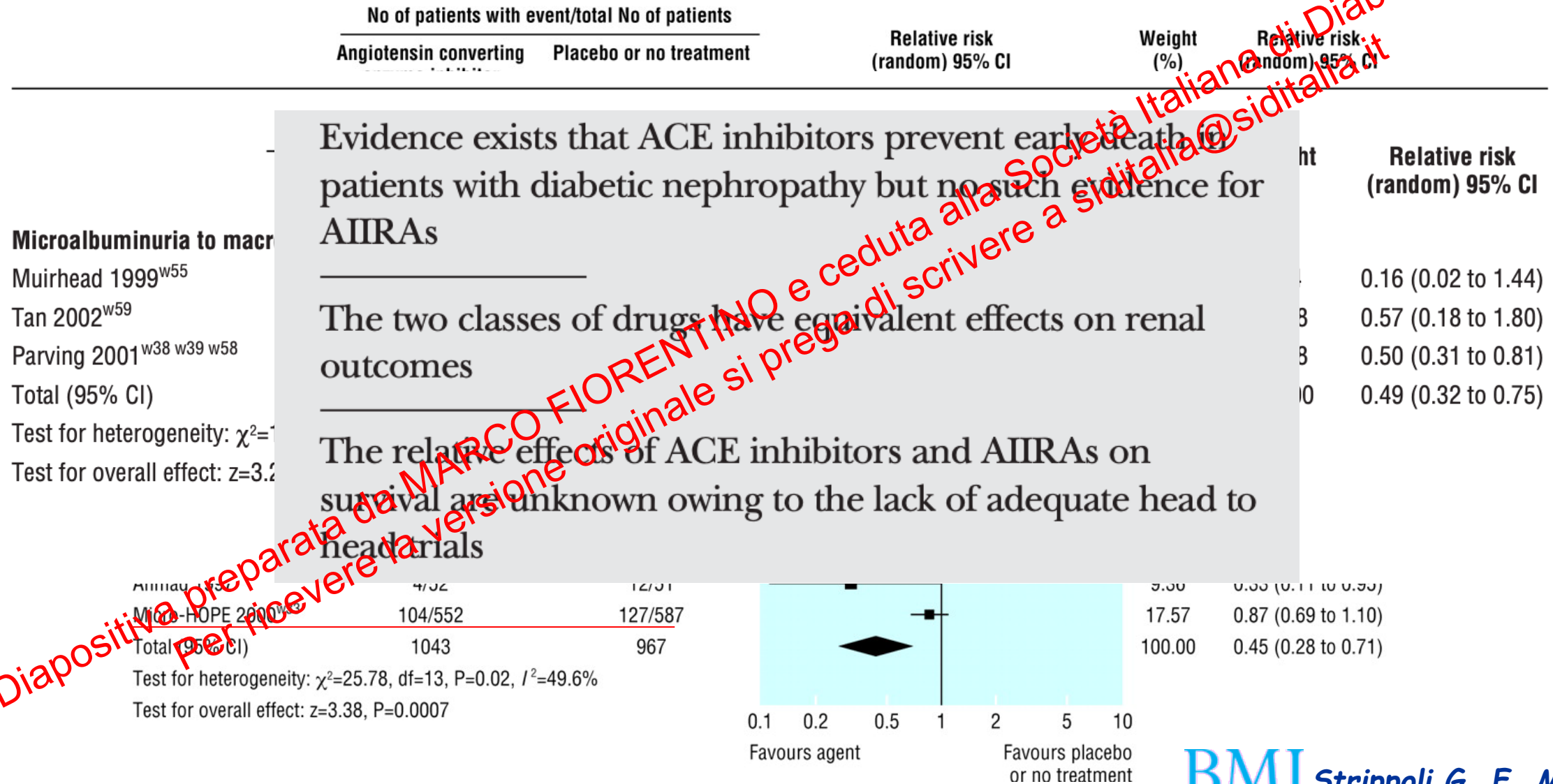
End Point	Perindopril- Indapamide (No. of Events/Patient [%])	Placebo	HR (95% CI)	P	NNT
Progression of nephropathy					
all renal events	1243/5569 (22.3)	1500/5571 (26.9)	0.79 (0.73 to 0.85)	<0.0001	20
progression of ≥ 1 albuminuria stage	<u>1179/5436 (21.7)</u>	1442/5412 (26.6)	0.78 (0.72 to 0.84)	<0.0001	18
new-onset microalbuminuria	1094/3995 (27.4)	1317/3991 (33.0)	0.79 (0.73 to 0.86)	<0.0001	16
new-onset macroalbuminuria	<u>114/5436 (2.1)</u>	163/5412 (3.0)	0.69 (0.54 to 0.88)	0.0027	97
patients with normoalbuminuria	25/3995 (0.6)	35/3991 (0.9)	0.71 (0.42 to 1.18)	0.1841	NA
patients with microalbuminuria	89/1441 (6.2)	128/1421 (9.0)	0.69 (0.52 to 0.91)	0.0074	32
doubling of serum creatinine >200 $\mu\text{mol/L}$	55/5569 (1.0)	45/5571 (0.8)	1.21 (0.81 to 1.79)	0.3483	NA
end-stage kidney disease ^b	25/5569 (0.4)	21/5571 (0.4)	1.18 (0.66 to 2.11)	0.5736	NA
Regression of nephropathy					
regression of ≥ 1 albuminuria stage	<u>908/1638 (55.4)</u>	816/1625 (50.2)	1.16 (1.06 to 1.28)	0.0017	19
regression to normoalbuminuria	<u>848/1638 (51.8)</u>	745/1625 (45.8)	1.15 (1.04 to 1.27)	0.0059	16
patients with microalbuminuria	797/1441 (55.3)	698/1421 (49.1)	1.15 (1.04 to 1.27)	0.0067	16
patients with macroalbuminuria	51/197 (25.9)	47/204 (23.0)	1.08 (0.72 to 1.60)	0.7146	NA

^aNA, not applicable; NNT, number needed to treat to prevent one event of nephropathy progression or to promote one event of nephropathy regression over 5 yr.

^bDefined as requirement of renal replacement therapy or renal death.

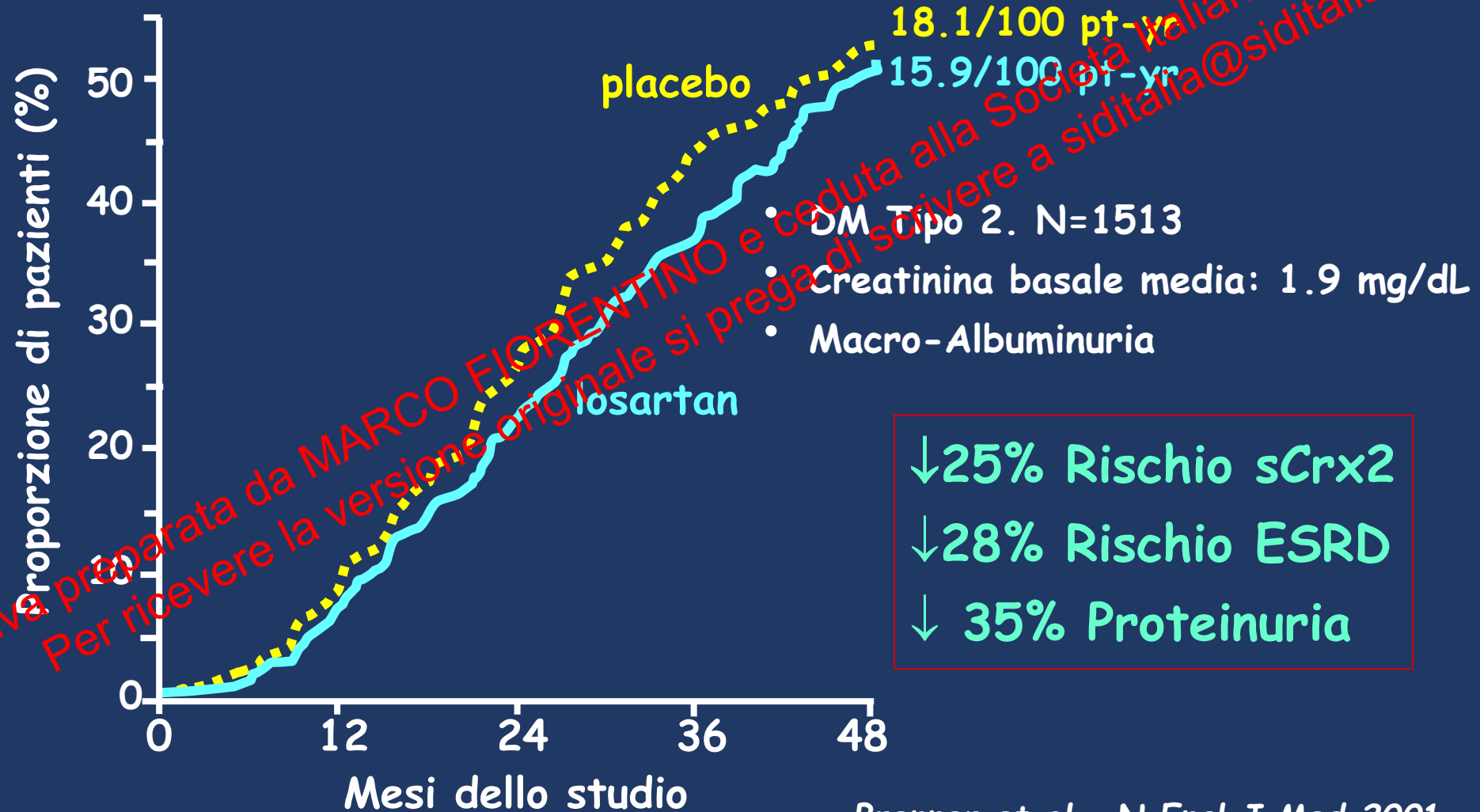
ACE-INIBITORI: Prevenzione Secondaria

risk of progression from microalbuminuria to macroalbuminuria



Sartani: Prevenzione Terziaria nel DM Tipo 2

STUDIO RENAAL

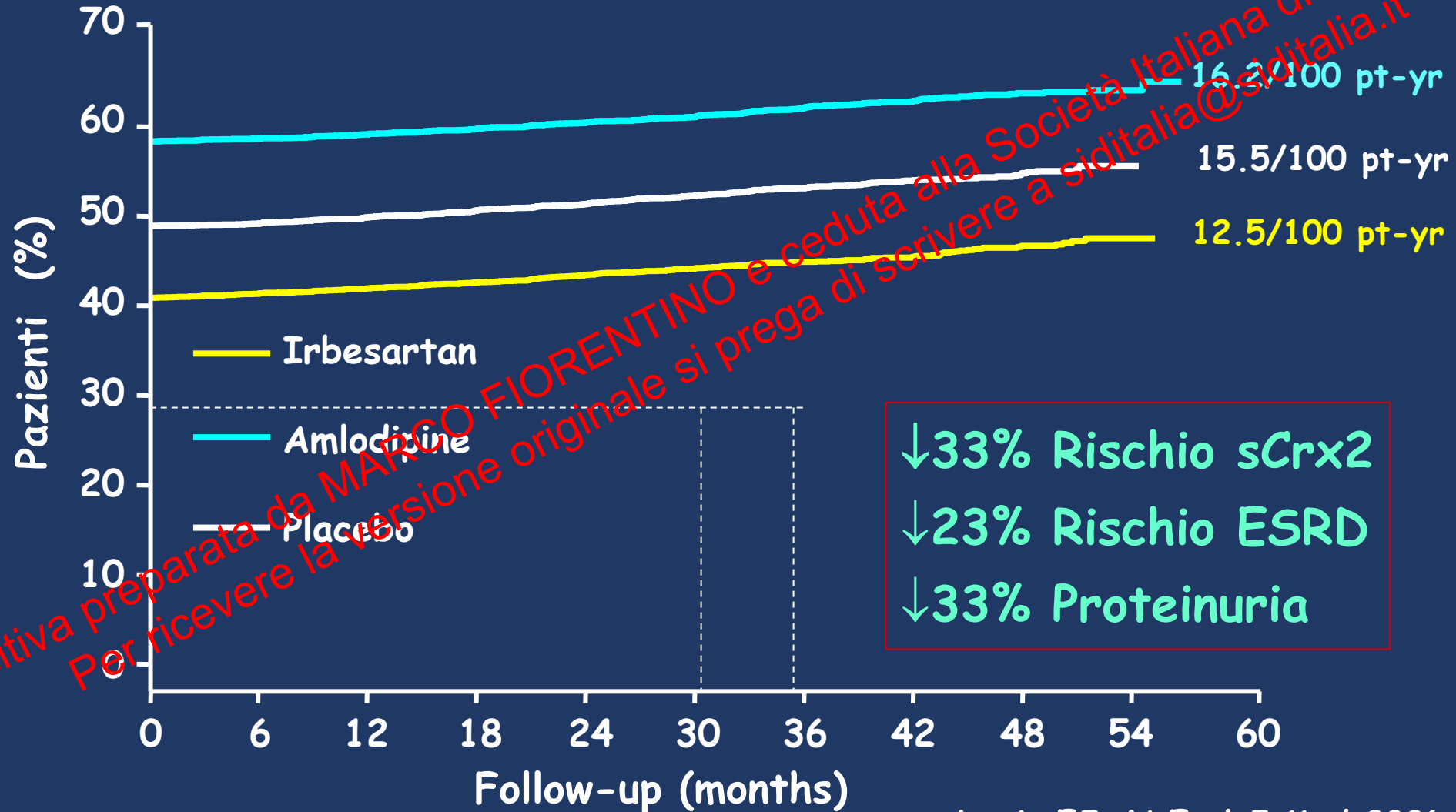


Brenner et al., N Engl J Med 2001

Sartani: Prevenzione Terziaria nel DM Tipo 2

- DM Tipo 2. N=1715

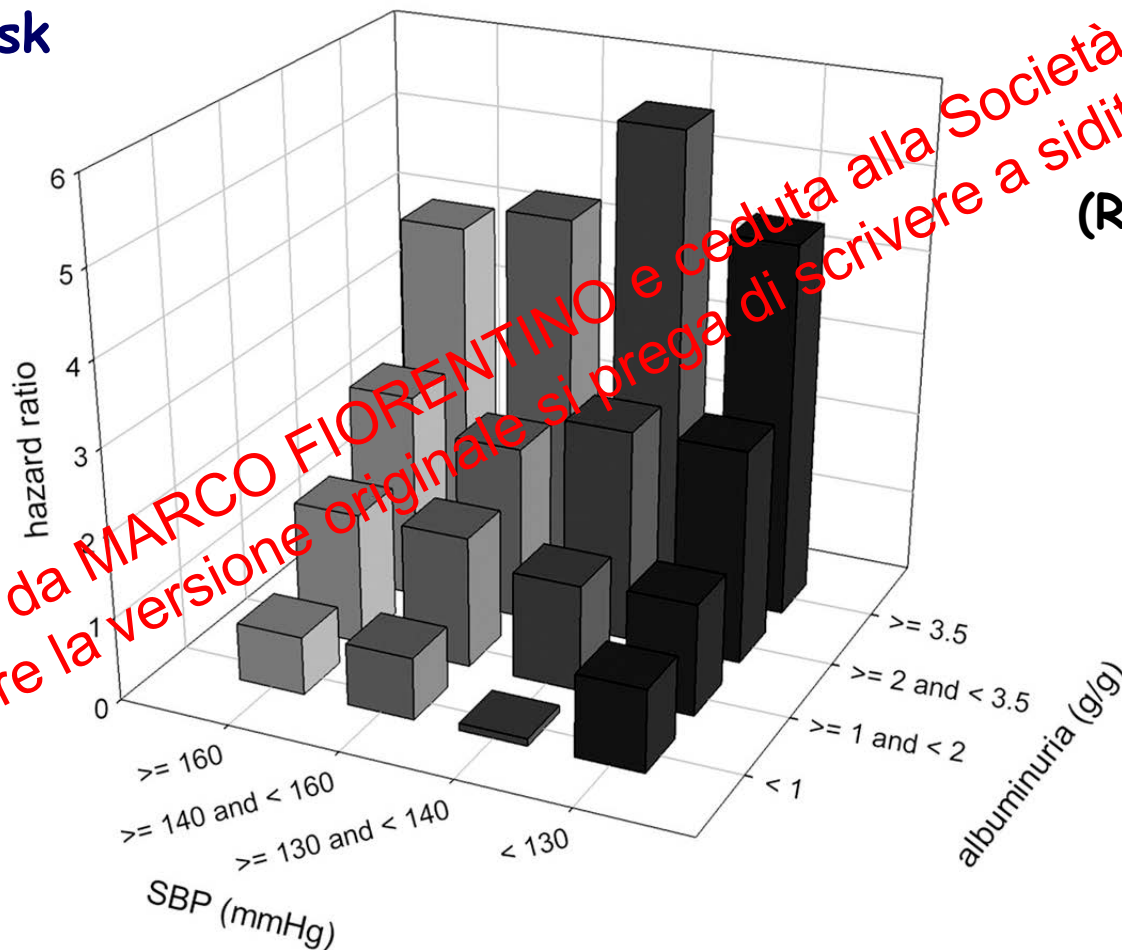
STUDIO IDNT



Lewis EJ, N Engl J Med 2001

L'Albuminuria è un obiettivo della reno-protezione indipendente dal controllo pressorio nei diabetici Tipo 2 con nefropatia

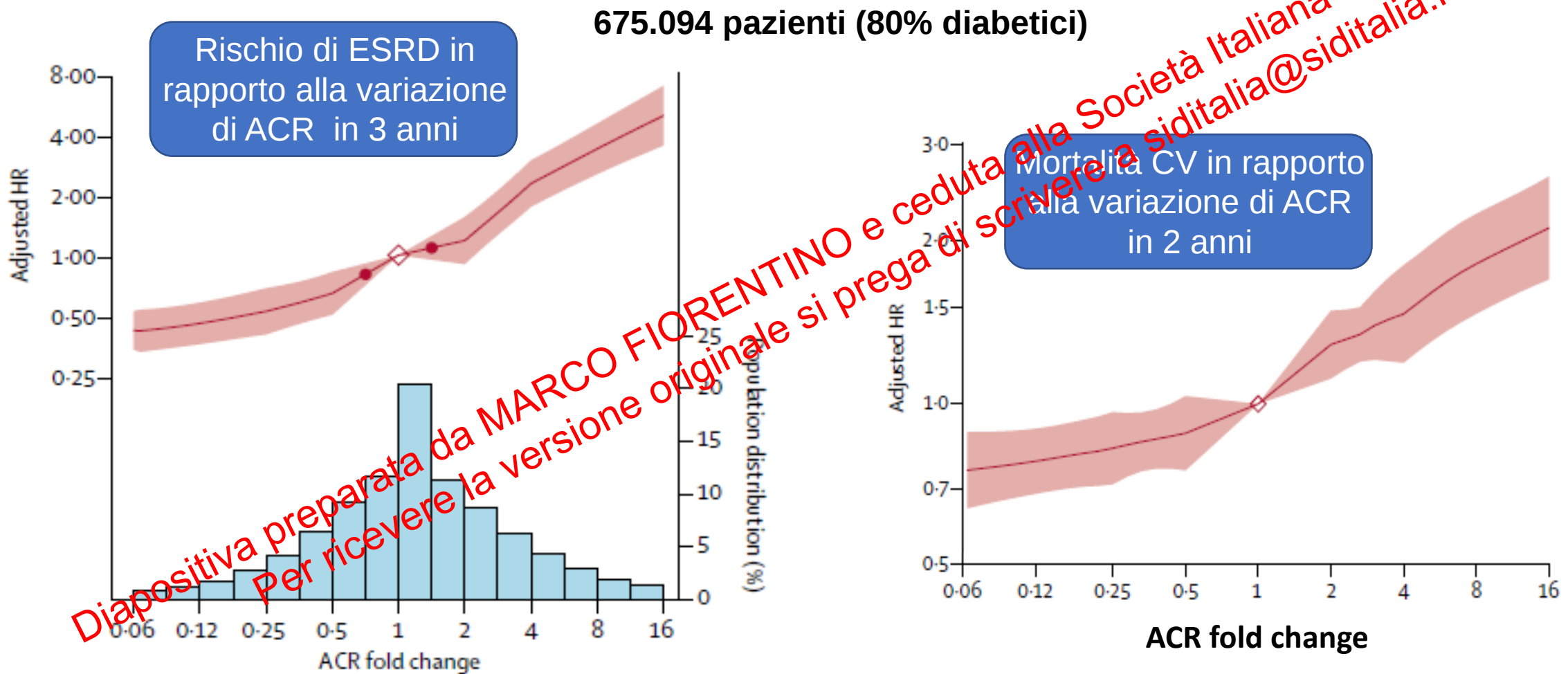
ESRD Risk



N=1428 Pts
(RENAAL Study)

Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

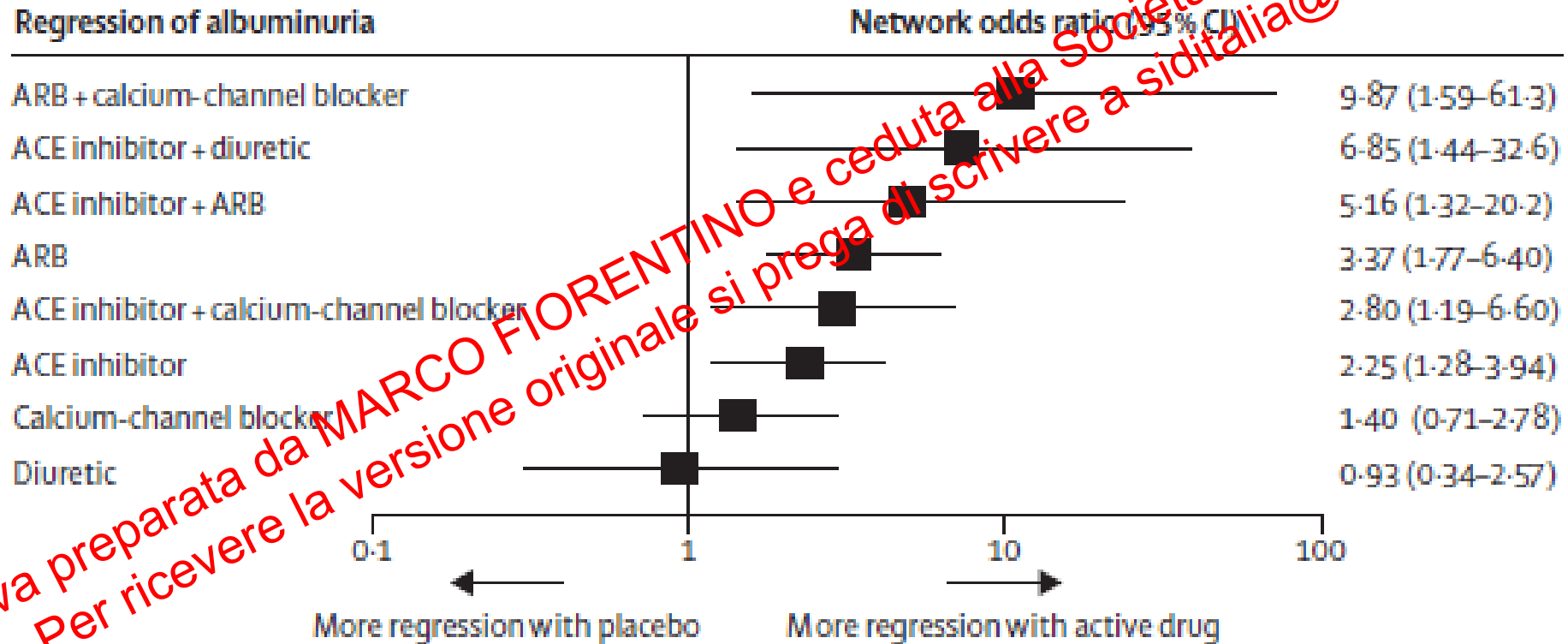
Change in albuminuria and subsequent risk of end-stage kidney disease: an individual participant-level consortium meta-analysis of observational studies



Comparative efficacy and safety of blood pressure-lowering agents in adults with diabetes and kidney disease: a network meta-analysis

Lancet 2015; 385: 2047-56

Suetonia C Palmer, Dimitris Mavridis, Eliano Navarese, Jonathan C Craig, Marcello Tonelli, Georgia Salanti, Natasha Wiebe, Mariella Ruospo, David C Wheeler, Giovanni F M Strippoli



Diapositiva preparata da MARCO FIORENTINO e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

Telmisartan, Ramipril, or Both in Patients at High Risk for Vascular Events

The ONTARGET Investigators*

Lo studio ONTARGET ha evidenziato che l'associazione ACEi + sartani

- a) si associa ad un minor declino del GFR rispetto ai pazienti trattati con telmisartan
- b) si associa a maggior incidenza di effetti negativi sulla funzione renale
- c) presenta significativi benefici clinici (outcome primario) rispetto alla monoterapia
- d) è consigliata nei pazienti ad alto rischio cardiovascolare

Telmisartan, Ramipril, or Both in Patients at High Risk for Vascular Events

The ONTARGET Investigators*

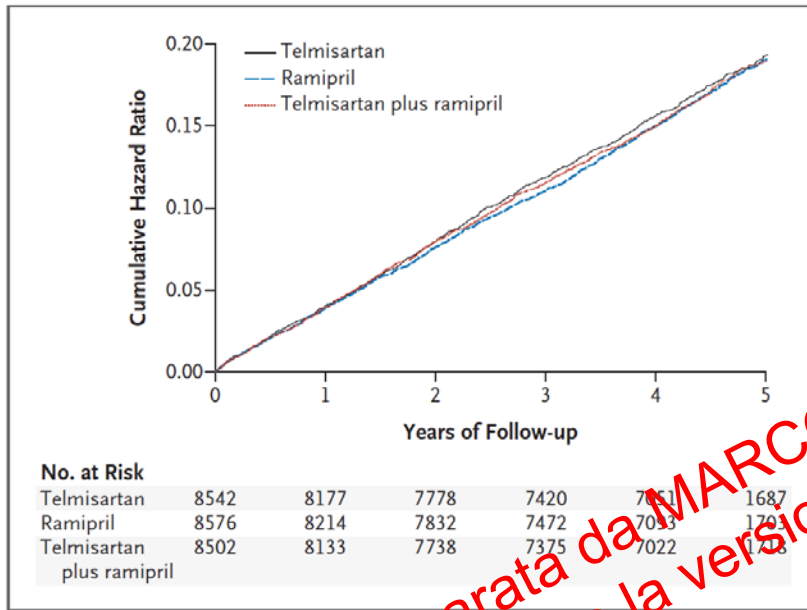


Figure 1. Kaplan-Meier Curves for the Primary Outcome in the Three Study Groups.

The composite primary outcome was death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure.

Table 4. Secondary and Other Outcomes.

Outcome	Ramipril (N=8576)	Telmisartan (N=8542)	Combination Therapy (N=8502)	Telmisartan vs. Ramipril	Combination Therapy vs. Ramipril
	number (percent)			relative risk (95% CI)	
Revascularization	1269 (14.8)	1290 (15.1)	1303 (15.3)	1.03 (0.95–1.11)	1.04 (0.97–1.13)
Hospitalization for angina	925 (10.8)	954 (11.2)	952 (11.2)	1.04 (0.95–1.14)	1.04 (0.95–1.14)
Worsening of new angina	567 (6.6)	536 (6.3)	538 (6.3)	0.95 (0.84–1.07)	0.96 (0.85–1.08)
New diagnosis of diabetes*	366 (6.7)	399 (7.5)	323 (6.1)	1.12 (0.97–1.29)	0.91 (0.78–1.06)
Any heart failure†	514 (6.0)	537 (6.3)	478 (5.6)	1.05 (0.93–1.19)	0.94 (0.83–1.07)
New atrial fibrillation‡	570 (6.9)	550 (6.7)	537 (6.5)	0.97 (0.86–1.09)	0.96 (0.85–1.07)
Renal impairment§	871 (10.2)	906 (10.6)	1148 (13.5)	1.04 (0.96–1.14)	1.33 (1.22–1.44)§
Renal failure requiring dialysis	48 (0.6)	52 (0.6)	65 (0.8)	1.09 (0.74–1.61)	1.37 (0.94–1.98)

Telmisartan was equivalent to ramipril in patients with vascular disease or high-risk diabetes and was associated with less angioedema. The combination of the two drugs was associated with more adverse events without an increase in benefit.

Cardiorenal End Points in a Trial of Aliskiren for Type 2 Diabetes

Hans-Henrik Parving, M.D., D.M.Sc., Barry M. Brenner, M.D., Ph.D., John J.V. McMurray, M.D., Dick de Zeeuw, M.D., Ph.D., Steven M. Haffner, M.D., Scott D. Solomon, M.D., Nish Chaturvedi, M.D., Frederik Persson, M.D., Akshay S. Desai, M.D., M.P.H., Maria Nicolaidis, M.D., Alexia Richard, M.Sc., Zhihua Xiang, Ph.D., Patrick Brunel, M.D., and Marc A. Pfeffer, M.D., Ph.D., for the ALTITUDE Investigators*

Table 3. Most Commonly Reported Adverse Events and Study-Drug Discontinuation.*

Event	Any Event Reported		P Value	Event Leading to Permanent Study-Drug Discontinuation	
	Aliskiren (N = 4272) no. of patients (%)	Placebo (N = 4285) no. of patients (%)		Aliskiren (N = 4272) no. of patients (%)	Placebo (N = 4285) no. of patients (%)
Hyperkalemia	1670 (39.1)	1244 (29.0)	<0.001	245 (5.8)	111 (2.6)
Peripheral edema	686 (16.1)	706 (16.5)	0.6	11 (0.3)	7 (0.2)
Hypotension	519 (12.1)	357 (8.3)	<0.001	28 (0.7)	13 (0.3)
Diarrhea	417 (9.8)	312 (7.3)	<0.001	1 (0.0)	7 (0.2)
Hypertension	429 (10.0)	409 (10.9)	0.17	3 (0.1)	9 (0.2)
Renal impairment	371 (8.8)	371 (8.7)	0.9	65 (1.5)	54 (1.3)
Nasopharyngitis	305 (9.5)	333 (8.0)	0.39	1 (<0.1)	0
Hypoglycemia	393 (9.2)	341 (8.0)	0.04	1 (<0.1)	3 (0.1)
Back pain	353 (8.3)	353 (8.2)	0.67	1 (<0.1)	2 (<0.1)
Dizziness	327 (7.7)	314 (7.3)	0.57	4 (0.1)	4 (0.1)
Urinary tract infection	326 (7.6)	288 (6.7)	0.10	4 (0.1)	2 (<0.1)
Anemia	316 (7.4)	307 (7.2)	0.68	0	0
Pain in extremities	302 (7.1)	317 (7.4)	0.56	1 (<0.1)	2 (<0.1)
Arthralgia	302 (7.1)	313 (7.3)	0.67	0	1 (<0.1)
Cough	265 (6.2)	283 (6.6)	0.45	1 (<0.1)	1 (<0.1)
Bronchitis	242 (5.7)	239 (5.6)	0.86	0	0
Dyspnea	223 (5.2)	213 (5.0)	0.60	6 (0.1)	5 (0.1)
Upper respiratory tract infection	223 (5.2)	229 (5.3)	0.80	1 (<0.1)	0
Cataract	229 (5.4)	223 (5.2)	0.75	0	0
Constipation	203 (4.8)	241 (5.6)	0.07	0	1 (<0.1)
Headache	200 (4.7)	220 (5.1)	0.33	2 (<0.1)	4 (0.1)

BACKGROUND

This study was undertaken to determine whether use of the direct renin inhibitor aliskiren would reduce cardiovascular and renal events in patients with type 2 diabetes and chronic kidney disease, cardiovascular disease, or both.

METHODS

In a double-blind fashion, we randomly assigned 8551 patients to aliskiren (300 mg daily) or placebo as an adjunct to an angiotensin-converting-enzyme inhibitor or an angiotensin-receptor blocker. The primary end point was a composite of the time to cardiovascular death or a first occurrence of cardiac arrest with resuscitation; nonfatal myocardial infarction; nonfatal stroke; unplanned hospitalization for heart failure; end-stage renal disease; death attributable to kidney failure, or the need for renal replacement therapy with no dialysis or transplantation available or initiated; or doubling of the baseline serum creatinine level.

RESULTS

The trial was stopped prematurely after the second interim efficacy analysis. After a median follow-up of 32.9 months, the primary end point had occurred in 783 patients (18.3%) assigned to aliskiren as compared with 732 (17.1%) assigned to placebo (hazard ratio, 1.08; 95% confidence interval [CI], 0.98 to 1.20; $P=0.12$). Effects on secondary renal end points were similar. Systolic and diastolic blood pressures were lower with aliskiren (between-group differences, 1.3 and 0.6 mm Hg, respectively) and the mean reduction in the urinary albumin-to-creatinine ratio was greater (between-group difference, 14 percentage points; 95% CI, 11 to 17). The proportion of patients with hyperkalemia (serum potassium level, ≥ 6 mmol per liter) was significantly higher in the aliskiren group than in the placebo group (11.2% vs. 7.2%), as was the proportion with reported hypotension (12.1% vs. 8.3%) ($P<0.001$ for both comparisons).

CONCLUSIONS

The addition of aliskiren to standard therapy with renin-angiotensin system blockade in patients with type 2 diabetes who are at high risk for cardiovascular and renal events is not supported by these data and may even be harmful. (Funded by Novartis; ALTITUDE ClinicalTrials.gov number, NCT00549757.)

Nefropatia Diabetica

Strategie Terapeutiche basate sull'evidenza

Strategia

Studio

- Controllo Metabolico Prevenz. primaria e secondaria
- ACE-I o ARB Prevenz. primaria, second. e terziaria
- BP < 130/80 Prevenzione terziaria (soprattutto)

Prevenzione Primaria=

Prevenzione della Microalbuminuria

Prevenzione Secondaria=

Prevenzione della Macroalbuminuria e IRC

Prevenzione Terziaria=

Prevenzione (rallentamento) dell'Uremia terminale