Continuità e complessità clinica: la medicina d'urgenza

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Azienda USL di Modena

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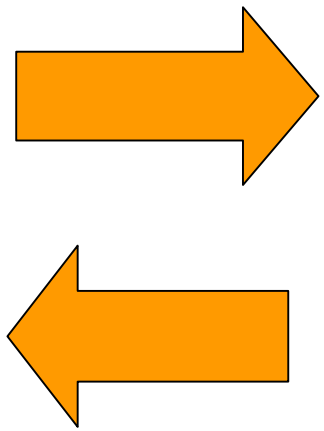
SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Modena

Complessità clinica



Complessità terapeutica

PRONTUARIO OSPEDALIERO (TERRITORIALE?)

È possibile trovare una essenzialità basata sull'evidenza?

SPECIALISTI OSPEDALIERI / MEDICI DI FAMIGLIA

Parlano spesso linguaggi diversi
Hanno spesso prospettive diverse

MA

Appartengono ad un’unica comunità

SPECIALISTI OSPEDALIERI / MEDICI DI FAMIGLIA

Condividono gli stessi obiettivi e aspettative

Dovrebbero avere le stesse evidenze

Dovrebbero possedere le stesse informazioni

Entrambi hanno le stesse pressioni economiche e commerciali

L'INDUSTRIA…

Novartis nel 2001 riporta una spesa pari al 36% del fatturato sotto la voce Marketing

Relman AS, Angell M, America's other drug problem
The New Republic 16, 2002 27-41

IL PAZIENTE…

…è spesso inteso come *‘customer’*
piuttosto che come
‘informed participant’…

CONTINUITA' OSPEDALE – TERRITORIO

Alleanza culturale tra i professionisti per promuovere la salute del paziente

"Continuity is coming up more and more as an important quality. And it's precisely that which is ignored and trampled on by marketed medicine. Shopping around is bad for everybody; it's bad for salesmen, too. We should not be salesmen."

Tudor Hart

David Brindle **Seeing red** BMJ, May **2007**; 334: **976** - 977

LO SPECIALISTA…

Prescrittore in dimissione ospedaliera

Prescrittore in Ambulatorio ospedaliero

PTO
=
strumento di supporto per la comunità medica contro una medicina di mercato

LO SPECIALISTA E L'INDUSTRIA

FARMACO RICHIESTO PER INSERIMENTO IN PTO	FARMACI PRESENTI IN PTO
ROSUVASTATINA	Simvastatina Pravastatina Atorvastatina
PERINDOPRIL	Captopril Ramipril Lisinopril
OLMESARTAN	Valsartan Candesartan Irbesartan

SONO DAVVERO INDISPENSABILI?

ATORVASTATINA

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Effects of High-Dose Atorvastatin on Cerebrovascular Events in Patients With Stable Coronary Disease in the TNT (Treating to New Targets) Study

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Philip Barter, MD, Jean-Charles Fruchart, PHD, Antonio M. Gotto, JR, MD, DPHIL, FACC,
Roddy Carter, MD, Andrei Breazna, PHD, John J. P. Kastelein, MD, PHD, Scott M. Grundy, MD, PHD

San Francisco, California; New York, New York; Sydney, Australia; Lille, France; Amsterdam, the Netherlands; and Dallas, Texas

OBJECTIVE We sought to assess the effects on cerebrovascular events of treating patients with stable coronary disease with low-density lipoprotein cholesterol (LDL-C) levels substantially below 100 mg/dl.

BACKGROUND Lowering LDL-C with statins has been shown to reduce the risk of stroke in patients with stable coronary disease. In observational studies, naturally low cholesterol levels have been associated with an increased risk of hemorrhagic stroke. The cerebrovascular benefits of treating patients with stable coronary disease to LDL-C levels substantially below 100 mg/dl have not been previously investigated.

METHODS We describe an analysis of cerebrovascular events in the Treating to New Targets study, a trial where 10,001 patients with documented coronary disease were randomized to treatment with atorvastatin at 10 mg/day or 80 mg/day and followed for a median of 4.9 years.

RESULTS Mean LDL-C levels were 101 mg/dl on 10 mg atorvastatin and 77 mg/dl on 80 mg. In addition to the reduction in major cardiovascular events (hazard ratio 0.78, 95% confidence interval [CI] 0.69 to 0.89; $p = 0.0002$), the primary end point of the trial, patients in the 80-mg arm experienced a reduction in cerebrovascular events (hazard ratio 0.77, 95% CI 0.64 to 0.93; $p = 0.007$) and stroke (hazard ratio 0.75, 95% CI 0.59 to 0.96; $p = 0.02$). Each 1-mg/dl reduction in LDL-C with treatment was associated with a 0.6% relative risk reduction in cerebrovascular events ($p = 0.002$) and a 0.5% relative risk reduction in stroke ($p = 0.041$). The incidence of hemorrhagic stroke was similar in the 80-mg and 10-mg groups, 16 and 18 respectively, and the hemorrhagic strokes were distributed evenly across quintiles of achieved LDL-C during treatment.

CONCLUSIONS Among patients with established coronary disease, treating to an LDL-cholesterol substantially below 100 mg/dl with 80 mg/day atorvastatin reduces both stroke and cerebrovascular events by an additional 20% to 25% compared with the 10 mg/day dose. An increase in hemorrhagic stroke was not seen at low LDL-C levels. (Treating to New Targets; http://www.clinicaltrials.gov; NCT00327691). (J Am Coll Cardiol 2006;48:1793–9)

JACC 2006; 48: 1793-9

ATORVASTATINA

Effect of High-Dose Atorvastatin on Hospitalizations for Heart Failure

Subgroup Analysis of the Treating to New Targets (TNT) Study

Kiran K. Khush, MD; David D. Waters, MD; Vera Bittner, MD; Prakash C. Deedwania, MD; John J.P. Kastelein, MD; Sandra J. Lewis, MD; Nanette K. Wenger, MD

Background—Statins reduce the rate of major cardiovascular events in high-risk patients, but their potential benefit as treatment for heart failure (HF) is less clear.

Methods and Results—Patients (n=10 001) with stable coronary disease were randomized to treatment with atorvastatin 80 or 10 mg/d and followed up for a median of 4.9 years. A history of HF was present in 7.8% of patients. A known ejection fraction <30% and advanced HF were exclusion criteria for the study. A predefined secondary end point of the study was hospitalization for HF. The incidence of hospitalization for HF was 2.4% in the 80-mg arm and 3.3% in the 10-mg arm (hazard ratio, 0.74; 95% confidence interval, 0.59 to 0.94; P=0.0116). The treatment effect of the higher dose was more marked in patients with a history of HF: 17.3% versus 10.6% in the 10- and 80-mg arms, respectively (hazard ratio, 0.59; 95% confidence interval, 0.4 to 0.88; P=0.009). Among patients without a history of HF, the rates of hospitalization for HF were much lower: 1.8% in the 80-mg group and 2.0% in the 10-mg group (hazard ratio, 0.87; 95% confidence interval, 0.64 to 1.16; P=0.34). Only one third of patients hospitalized for HF had evidence of preceding angina or myocardial infarction during the study period. Blood pressure was almost identical during follow-up in the treatment groups.

Conclusions—Compared with a lower dose, intensive treatment with atorvastatin in patients with stable coronary disease significantly reduces hospitalizations for HF. In a post hoc analysis, this benefit was observed only in patients with a history of HF. The mechanism accounting for this benefit is unlikely to be due primarily to a reduction in interim coronary events or differences in blood pressure. (***Circulation.*** **2007;115:576-583.)**

Key Words: atorvastatin ■ cholesterol ■ coronary disease ■ heart failure ■ hospitalizations ■ lipids ■ statins

Circulation 2007; 115: 576-83

ATORVASTATINA: BENEFICI vs RISCHI

Atorvastatin, 80 mg/d vs 10 mg/d, for preventing cerebrovascular events in stable coronary heart disease at median 4.9 years‡

Outcomes	Atorvastatin 80 mg/d	Atorvastatin 10 mg/d	RRR (95% CI)	NNT (CI)
Cerebrovascular event	3.9%	5.0%	23% (7 to 35)	89 (57 to 293)
Stroke	2.3%	3.1%	25% (14 to 41)	131 (80 to 234)
Transient ischemic attack	1.7%	2.2%	21% (–5 to 40)	Not significant
			RRI (CI)	**NNH (CI)**
Adverse events	8.1%	5.8%	41% (22 to 63)	43 (30 to 74)

‡Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from hazard ratios and data in article.

SONO DAVVERO BENEFICI ESSENZIALI RISPETTO A RISCHI CONCRETI?

ACP J Club. 2007 Mar-Apr;146(2):30.

ATORVASTATINA

Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial

*Helen M Colhoun, D John Betteridge, Paul N Durrington, Graham A Hitman, H Andrew W Neil, Shona J Livingstone, Margaret J Thomason, Michael I Mackness, Valentine Charlton-Menys, John H Fuller, on behalf of the CARDS investigators**

Lancet 2004; 364: 685–96

See Comment page 641

Lancet 2004; 364: 685-96

ATORVASTATINA

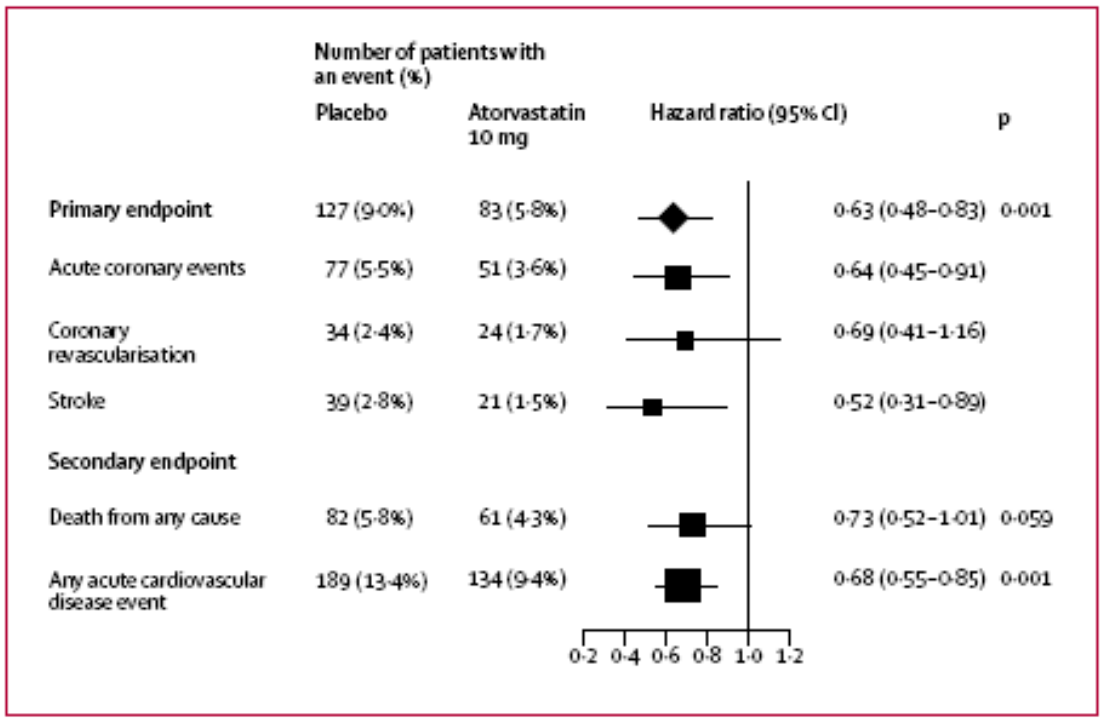

Figure 3: **Effect of treatment on primary and secondary endpoints**
Total number of acute coronary events, coronary revascularisations, and strokes separately do not equal the total number of primary events shown above, because only the first of these events is included in the primary endpoint. Thus, an individual who has had a stroke and a revascularisation will be counted only once in the primary endpoint but will appear in both separate totals for revascularisation and stroke. Symbol size is proportional to amount of statistical information.

Lancet 2004; 364: 685-96

ATORVASTATINA

Efficacy and Safety of Atorvastatin in the Prevention of Cardiovascular End Points in Subjects With Type 2 Diabetes

The Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus (ASPEN)

Robert H. Knopp, MD[1]
Michael d'Emden, MD[2]
Johan G. Smilde, MD, PhD[3]
Stuart J. Pocock, PhD[4]
on behalf of the ASPEN Study Group*

Diabetes Care 29:1478–1485, 2006

Diabetes Care 2006; 29: 1478-85

ATORVASTATINA

Atorvastatin vs placebo for type 2 diabetes at median 4 years‡

Outcomes	Atorvastatin	Placebo	RRR (95% CI)	NNT
Composite endpoint§	14% (166/1211)	15% (180/1199)	10% (–12 to 27)	Not significant
Fatal or nonfatal MI	4.0%	5.5%	27% (–6 to 49)	Not significant

‡MI = myocardial infarction. Other abbreviations defined in Glossary; individual event rates of the composite endpoint, RRR, NNT, and CI provided by author.
§Cardiovascular death (3.1% vs 3.1%), nonfatal MI (3.5% vs 4.8%), nonfatal stroke (2.6% vs 3.0%), recanalization (3.6% vs 3.9%), coronary artery bypass grafting (4.0% vs 4.1%), resuscitated cardiac arrest, or worsening or unstable angina requiring hospitalization (3.1% vs 3.0%).

EVIDENZE SCIENTIFICHE O PRESSIONI COMMERCIALI?

Diabetes Care 2006; 29: 1478-85

INIBITORI COX-2

Combination of a cyclo-oxygenase-2 inhibitor and a proton-pump inhibitor for prevention of recurrent ulcer bleeding in patients at very high risk: a double-blind, randomised trial

Francis Ka Leung Chan, Vincent Wai Sun Wong, Bing Yee Suen, Justin Che Yuen Wu, Jessica Yuet Ling Ching, Lawrence Cheung Tsui Hung, Aric Josun Hui, Vincent King Sun Leung, Vivian Wing Yan Lee, Larry Hin Lai, Grace Lai Hung Wong, Dorothy Kai Lai Chow, Ka Fa To, Wai Keung Leung, Philip Wai Yan Chiu, Yuk Tong Lee, James Yun Wong Lau, Henry Lik Yuen Chan, Enders Kwok Wai Ng, Joseph Jao Yiu Sung

Interpretation Patients at very high risk for recurrent ulcer bleeding who need anti-inflammatory analgesics should receive combination treatment with a COX 2 inhibitor and a PPI. Our findings should encourage guideline committees to review their recommendations for patients at very high risk of recurrent ulcer bleeding.

DAVVERO DOBBIAMO CAMBIARE LE LG SULLA BASE DI UN SINGOLO TRIAL?
ATTUALMENTE LA NOTA CUF NEGA LA DISPENSABILITÀ…

Lancet 2007; 369: 1621-26

PIOGLITAZONE

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

John A Dormandy, Bernard Charbonnel, David J A Eckland, Erland Erdmann, Massimo Massi-Benedetti, Ian K Moules, Allan M Skene, Meng H Tan, Pierre J Lefèbvre, Gordon D Murray, Eberhard Standl, Robert G Wilcox, Lars Wilhelmsen, John Betteridge, Kåre Birkeland, Alain Golay, Robert J Heine, László Korányi, Markku Laakso, Marián Mokáň, Antanas Norkus, Valdis Pirags, Toomas Podar, André Scheen, Werner Scherbaum, Guntram Schernthaner, Ole Schmitz, Jan Škrha, Ulf Smith, Jan Taťoň, on behalf of the PROactive investigators*

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.

Lancet 2005; 366: 1279-89

PIOGLITAZONE: I BENEFICI

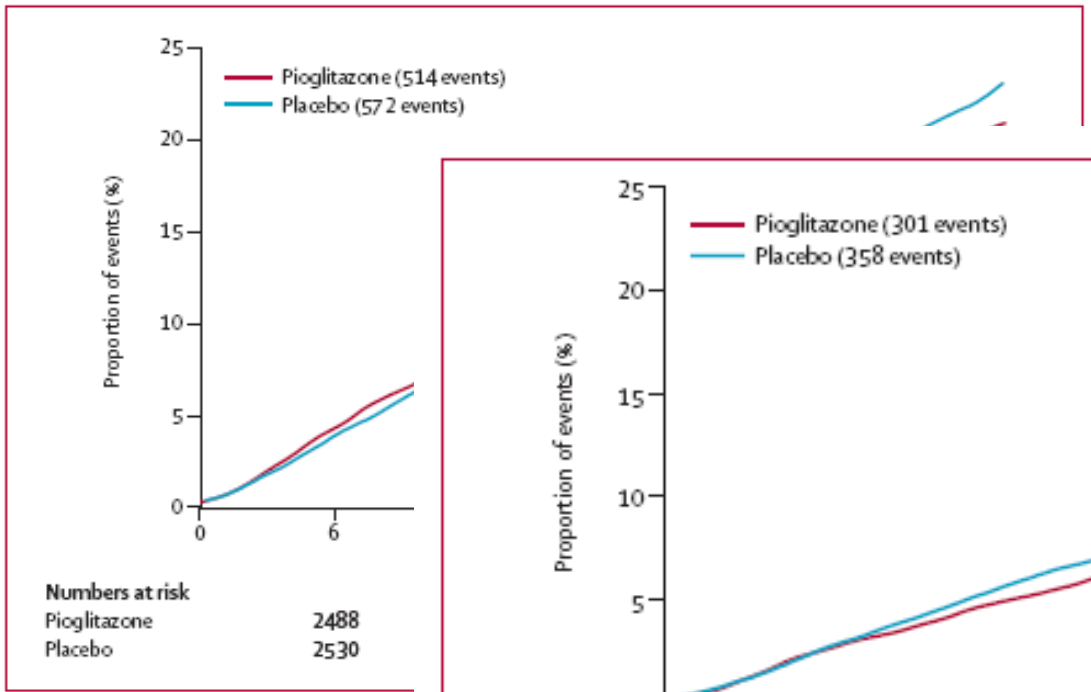

Figure 2: Kaplan-Meier curve of time to pri
*Death from any cause, non-fatal myocardia
coronary syndrome, leg amputation, corona

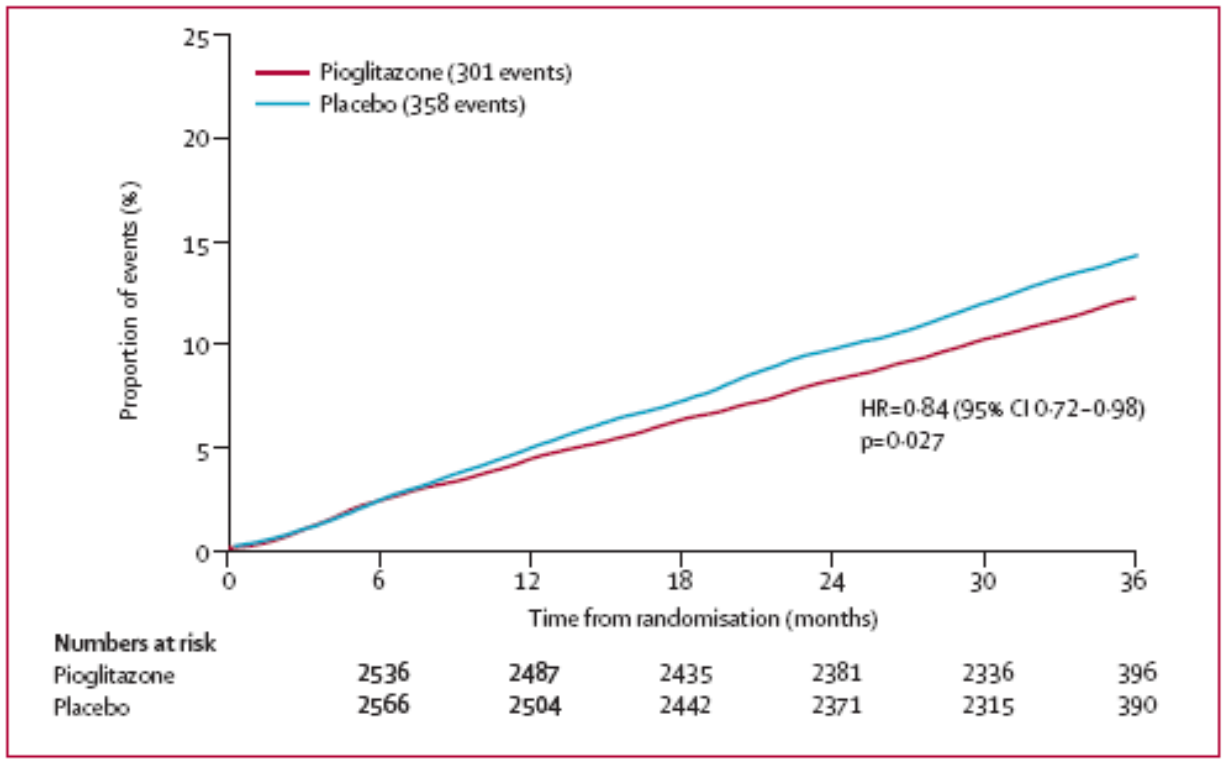

Figure 3: Kaplan-Meier curve of time to main secondary endpoint*
*Death from any cause, non-fatal myocardial infarction (excluding silent myocardial infarction), or stroke.

Lancet 2005; 366: 1279-89

PIOGLITAZONE: I RISCHI

	Pioglitazone (n=2605)		Placebo (n=2633)		p
	Number of events	Number of patients	Number of events	Number of patients	
Any report of heart failure*	417	281 (11%)	302	198 (8%)	<0·0001
Heart failure not needing hospital admission*	160	132 (5%)	117	90 (3%)	0·003
Heart failure needing hospital admission*	209	149 (6%)	153	108 (4%)	0·007
Fatal heart failure†	25	25 (1%)	22	22 (1%)	0·634

*Not adjudicated. †Adjudicated cause of death.

Table 9: Reports of heart failure

Lancet 2005; 366: 1279-89

PIOGLITAZONE: I RISCHI

Pioglitazone (Piog) v placebo for type 2 diabetes and macrovascular events*

Outcomes at mean 34.5 months	Piog	Placebo	RRR (95% CI)	NNT (CI)
Primary composite end point†	20%	22%	9.2% (−0.9 to 18)	Not significant
Main secondary composite endpoint†	12%	14%	15% (1.9 to 26)	49 (27 to 407)
Any serious adverse event	46%	48%	4.6% (−1.1 to 9.9)	Not significant
			RRI (CI)	**NNH (CI)**
Heart failure	11%	8%	40% (22 to 60)	23 (16 to 38)

*Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.
†See website (www.evidence-basedmedicine.com) for component event rates.

Evid Based Med. 2006 Apr;11(2):47

CONCLUSIONI

- Occorre lavorare su prontuari locali
- Le linee guida possono essere condizionate dall'industria
- Esistono molte pressioni commerciali
- Lo specialista deve lavorare insieme al *non* specialista


PORCUPINE
DANCE STEPS
OUCH!
NEW DRUGS
PROMOTIONAL
BALL
SUE SHAPLES