

GLP1 e sistema cardiovascolare; fisiologia

Diapositiva preparata da Gianluca Perseghin e ceduta alla Società Italiana di Diabetologia.
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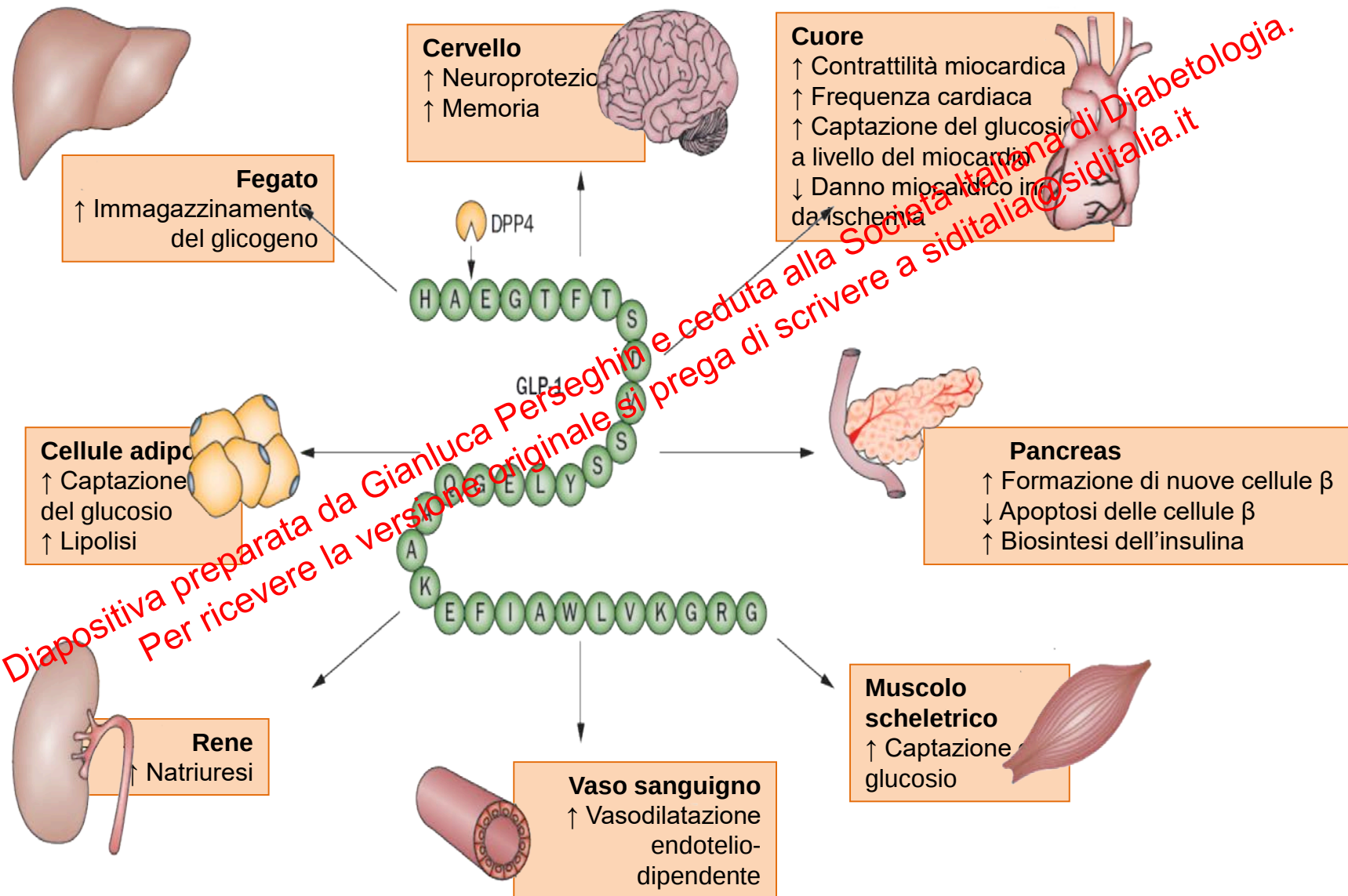


Gianluca Perseghin

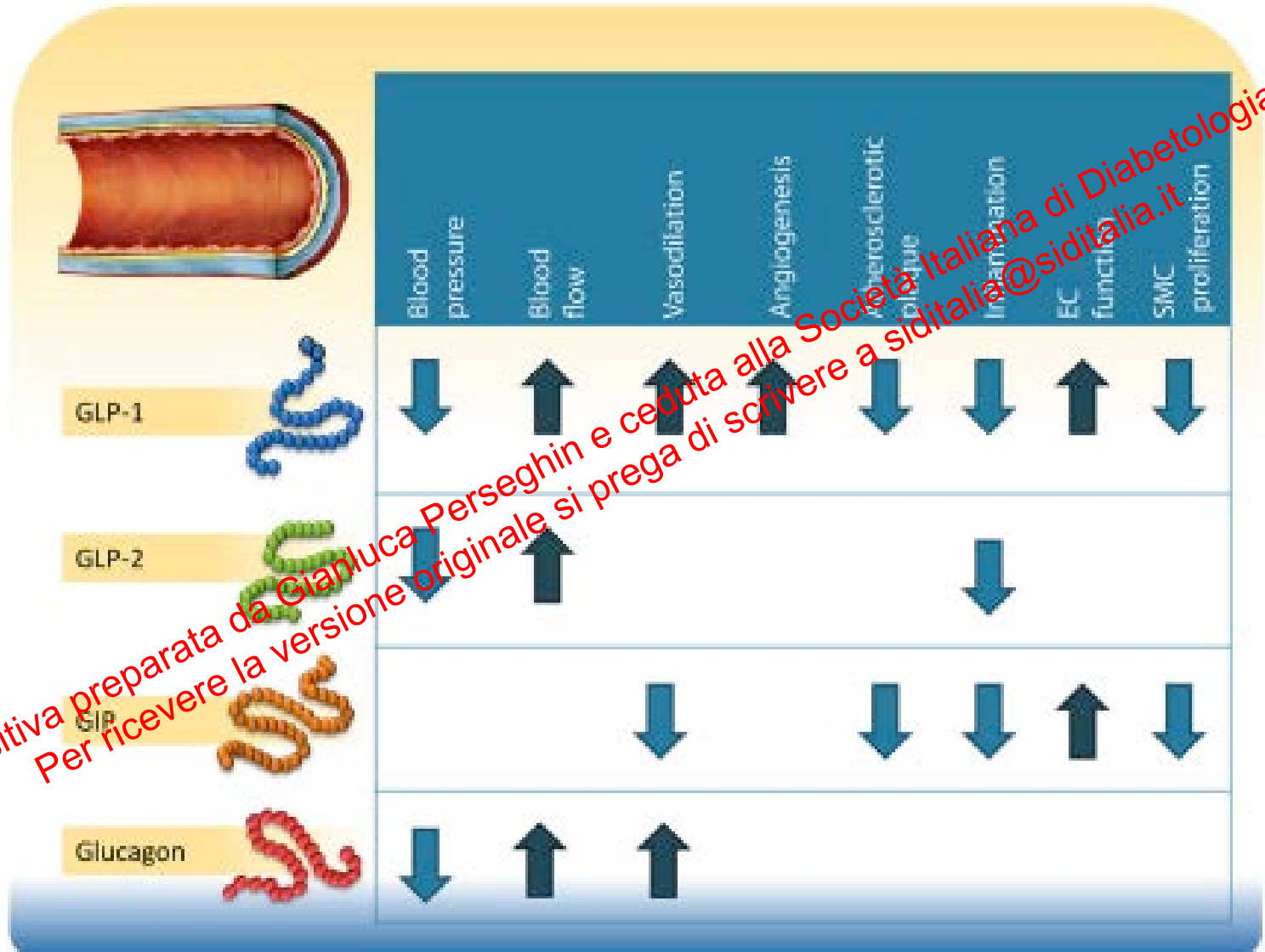


GLP-1: UN AMPIO SPRETTO DI AZIONI BIOLOGICHE

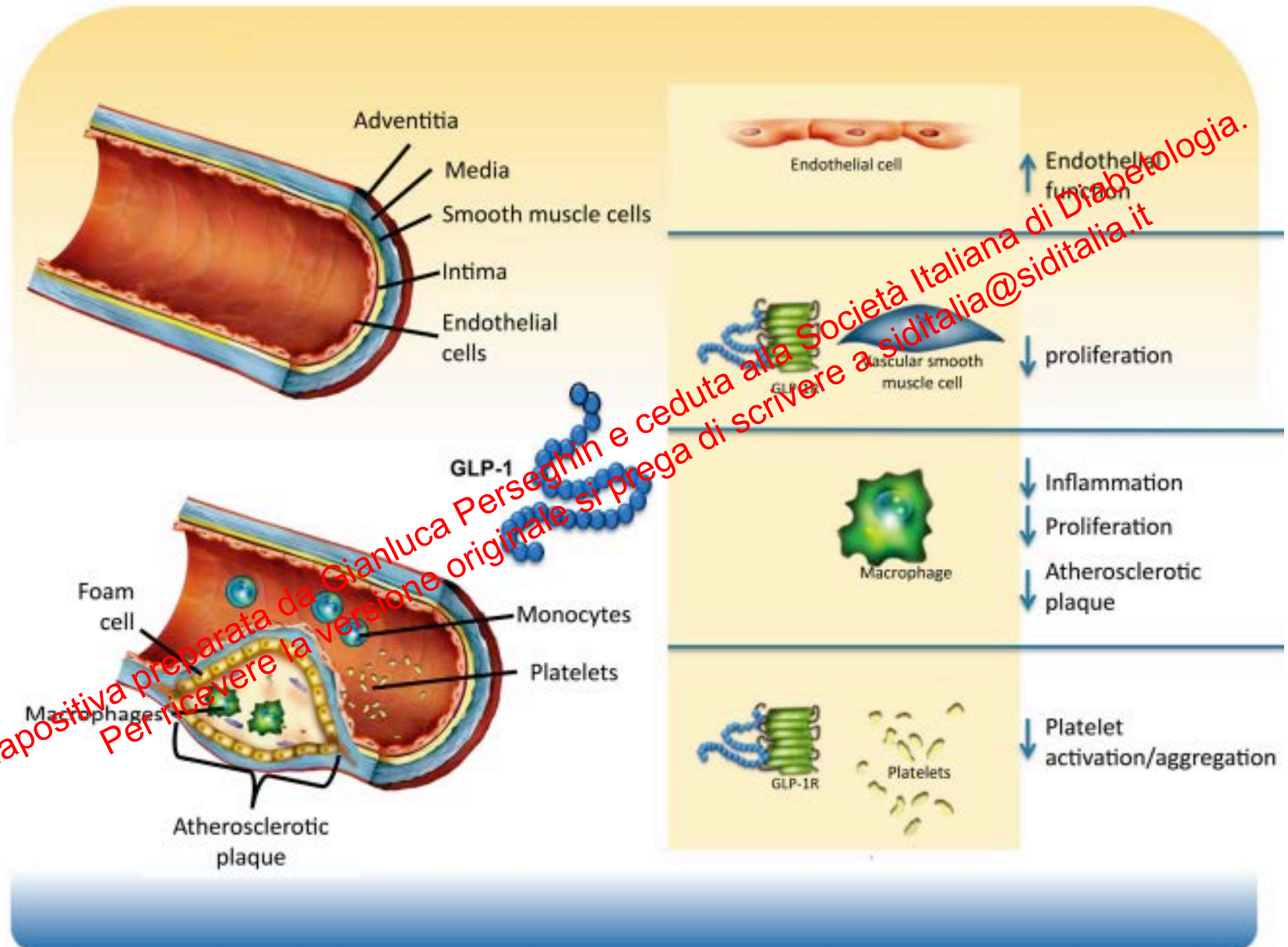
Meier JJ. Nat Rev Endocrinol 2012



Effetti CV delle Incretine

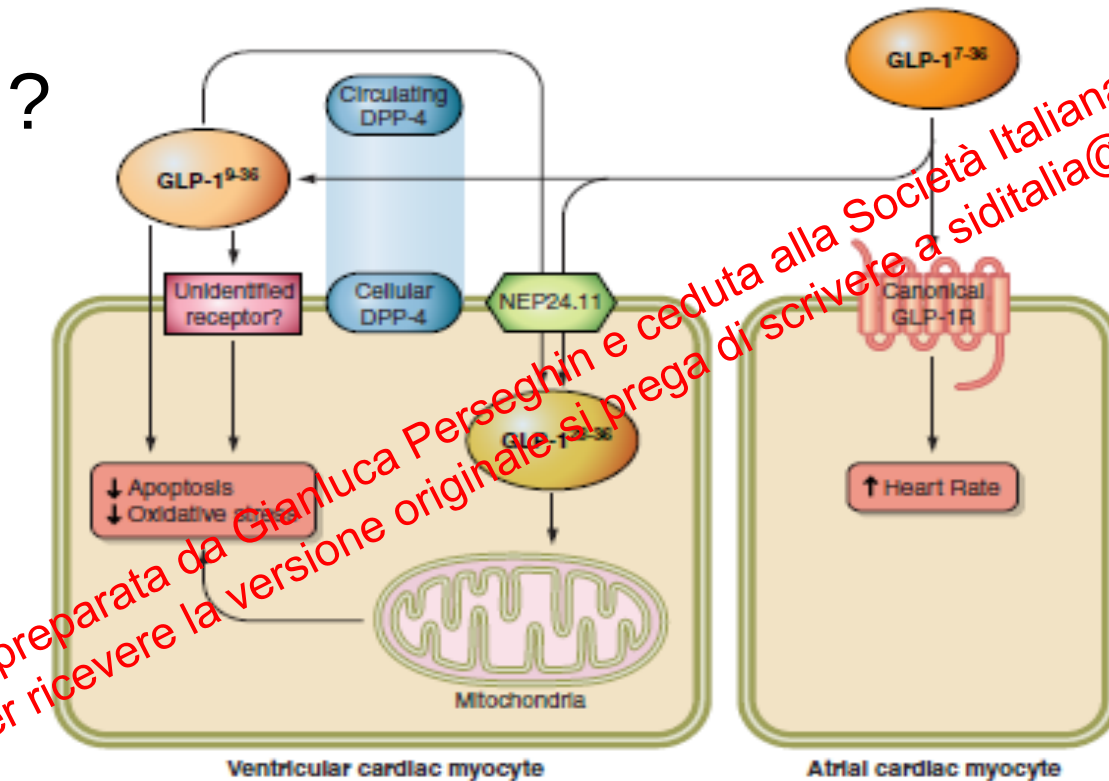


Effetti CV del GLP-1 sui Meccanismi dell'Aterosclerosi



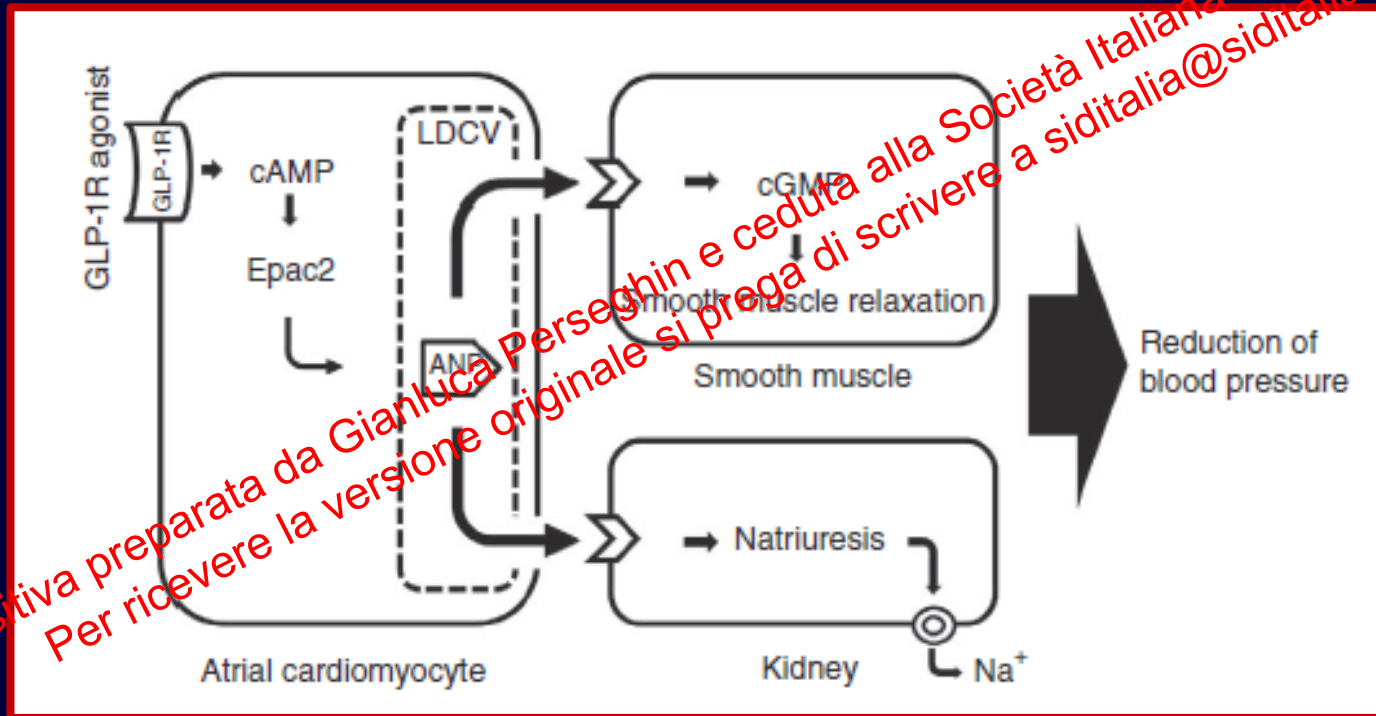
Myocardial effect of GLP1

Potential GLP-1-mediated actions in atrial and ventricular cardiac myocytes



GLP1RAs stimulate cardiomyocyte's ANP release

Glp1r mRNA transcripts are localized predominantly to the atria

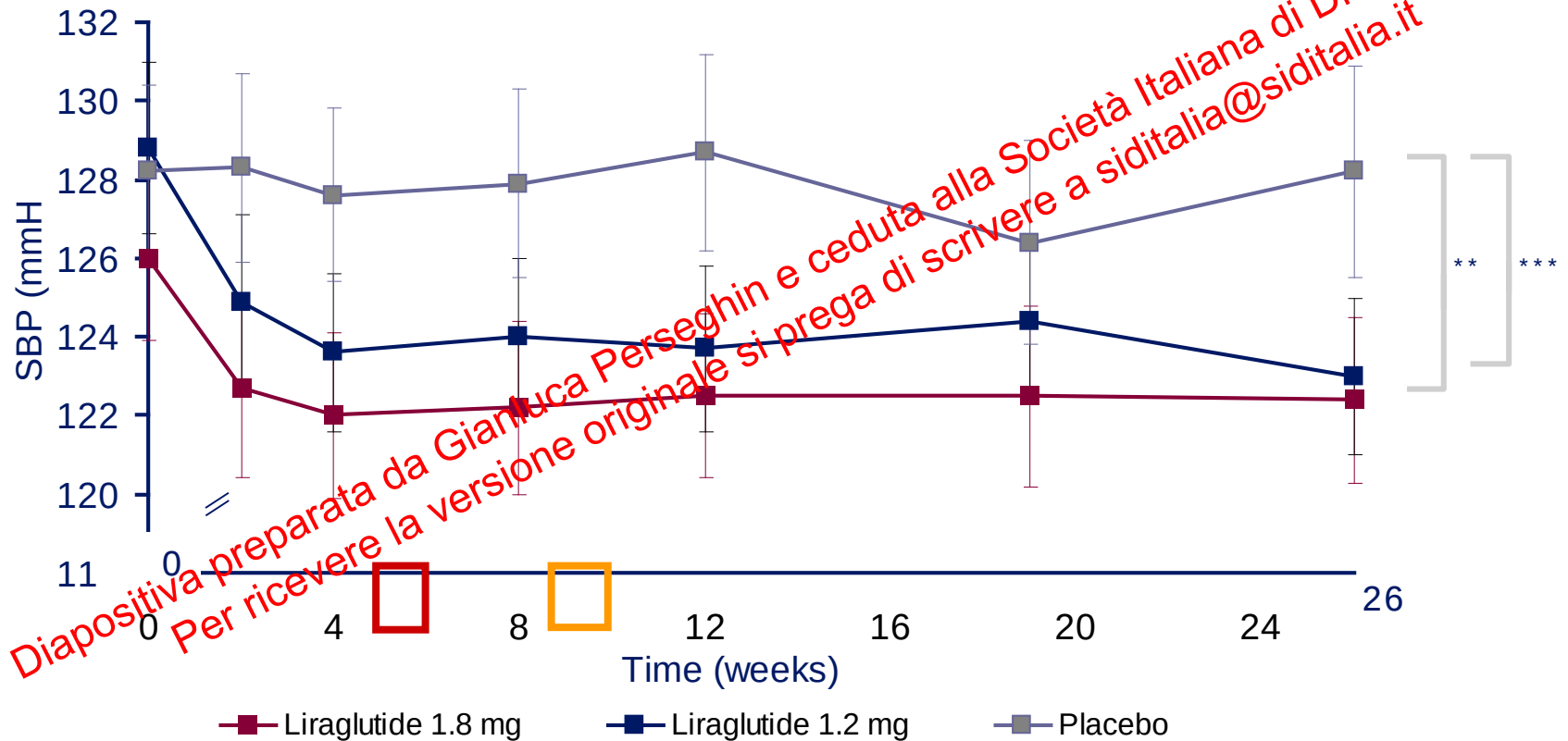


Epac2 (also known as Rapgef4) ?

GLP1 RA Cardiovascular risk factors

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Liraglutide and blood pressure



settimane riduzione pressione arteriosa
settimane riduzione peso corporeo

Zinman B *et al. Diabetes Care*, 2009

Effects of exenatide and liraglutide on heart rate, blood pressure and body weight: systematic review and meta-analysis

Louise E Robinson,¹ Tim A Holt,^{1,2} Karen Rees,¹ Harpal S Randeva,¹ Joseph P O'Hare¹

Systolic blood pressure decreased

1) -1.79 mm Hg (-2.94 to -0.64) vs. placebo

2) -2.39 mm Hg (-3.35 to -1.42) vs. active control

Heart rate increased

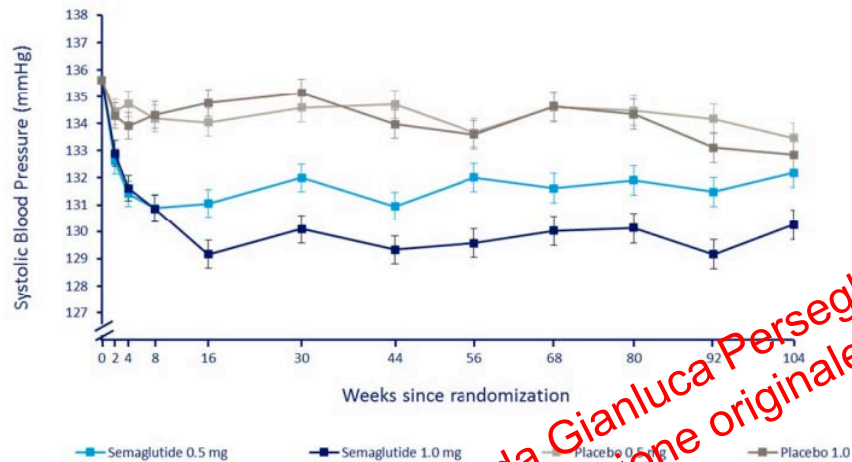
1) 1.86 bpm (0.85 to 2.87) vs. placebo

2) 1.90 bpm (1.30 to 2.50) vs. active control

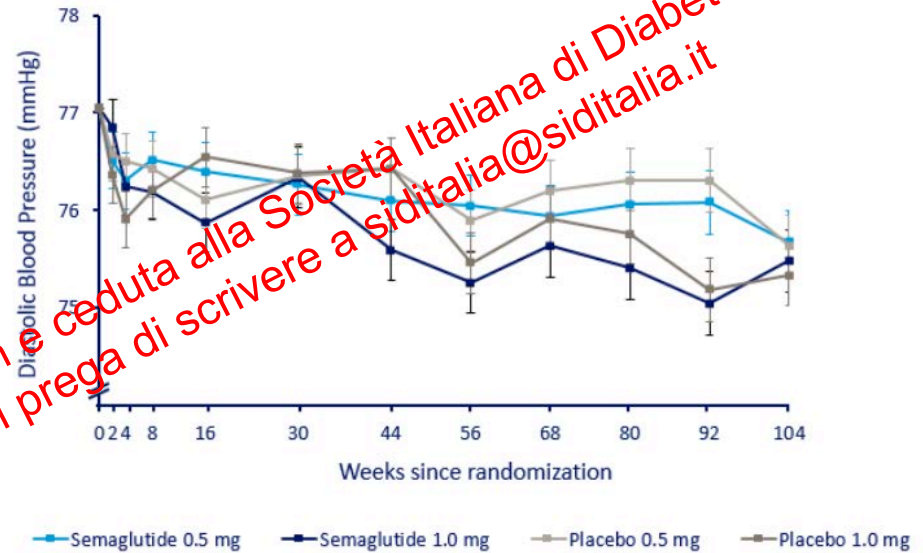
more evident for liraglutide and exenatide long-acting release than for exenatide twice daily

Blood Pressure in SUSTAIN-6

A. Systolic blood pressure



B. Diastolic blood pressure



Marso et al N Engl J Med, 2016

GLP-1 RA & Cardioprotective Effects

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A role for GLP1R agonism ?

- 1) GLP-1 receptors have been demonstrated in cardiac Myocytes. Yamamoto H et al J Clin Invest 2002

Data in animal models

- 2) GLP-1 may enhance recovery of LV function after transient coronary artery occlusion in an isolated rat heart model
Bose AK et al Cardiovasc Drugs Ther 2005

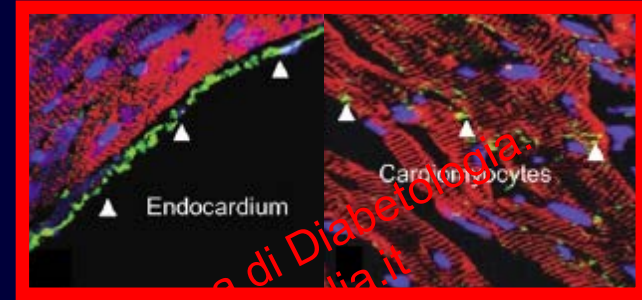
- 3) Beneficial outcomes were reported in the dog model of pacing-induced dilated cardiomyopathy Nikolaidis LA et al Circulation, 2004

Data in humans

- 4) GLP-1 infusion over 72 hours to 10 patients with acute myocardial infarction and depressed LV ejection fractions (40%) after successful primary coronary intervention had better short term cardiac outcomes in comparison with 11 contemporary control patients

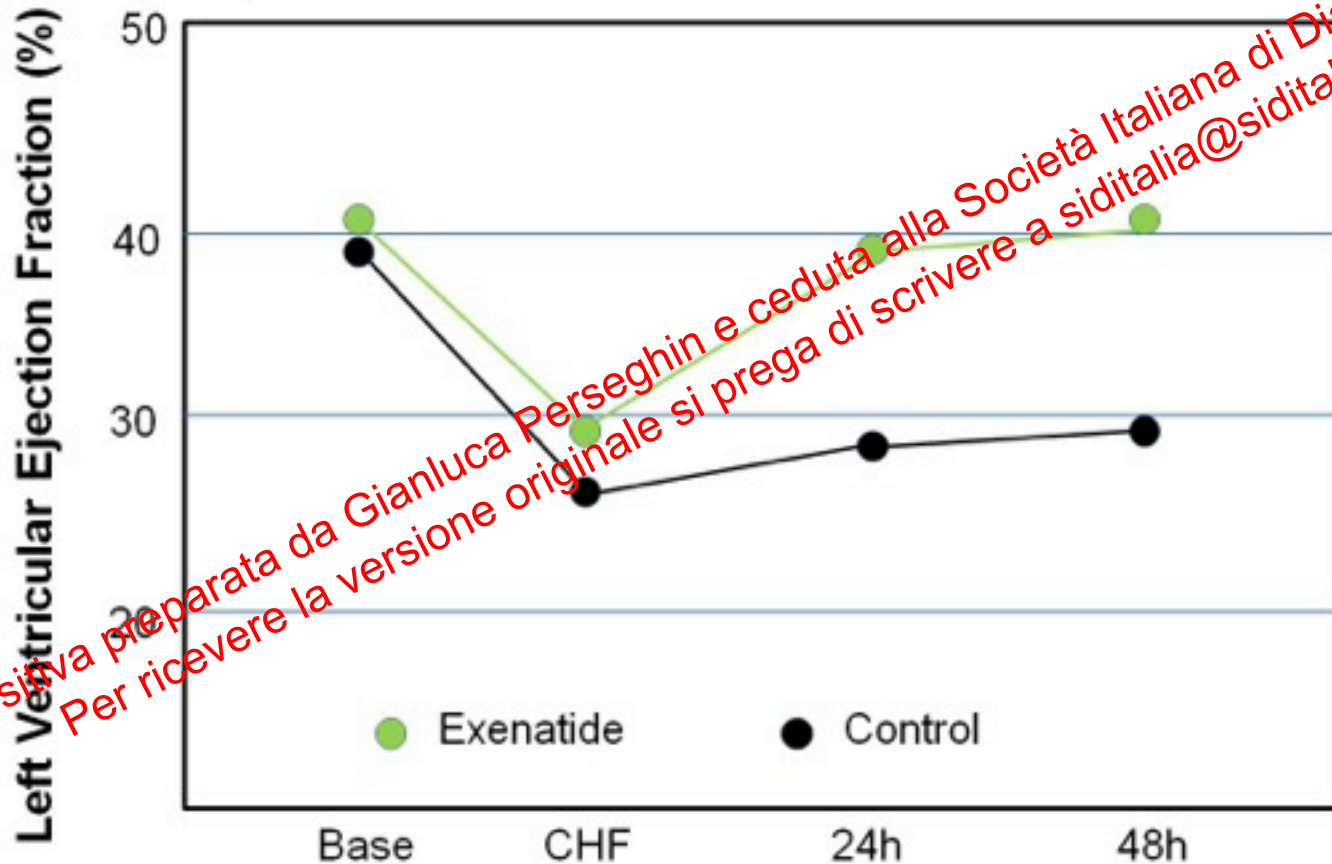
Nikolaidis LA et al Circulation, 2004

- 5) Administration of a 5-week infusion of GLP-1 to 12 patients with advanced HF significantly improved LV ejection fraction and VO2max in comparison with patients on standard therapy
Sokos GG et al J Card Fail, 2006



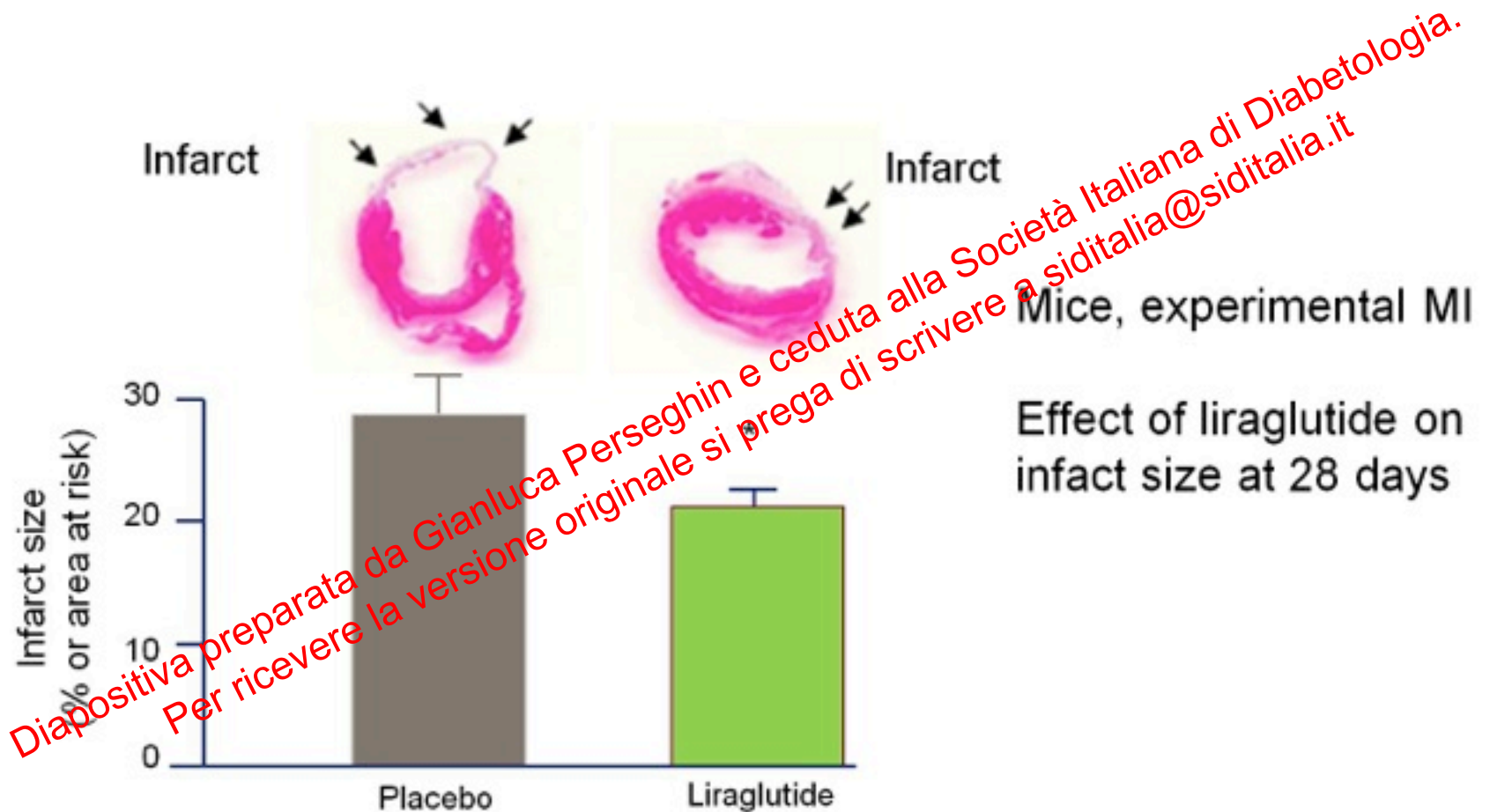
Myocardial effects of GLP1

Effect of exenatide on cardiac function in dogs with pacing-induced dilated cardiomyopathy



Nikolaidis LA et al. *Circulation* 2004; 110:955-961.

Myocardial effects of GLP1



Myocardial effects of GLP1

- Porcine model of ischaemia-reperfusion injury; effect of Exenatide



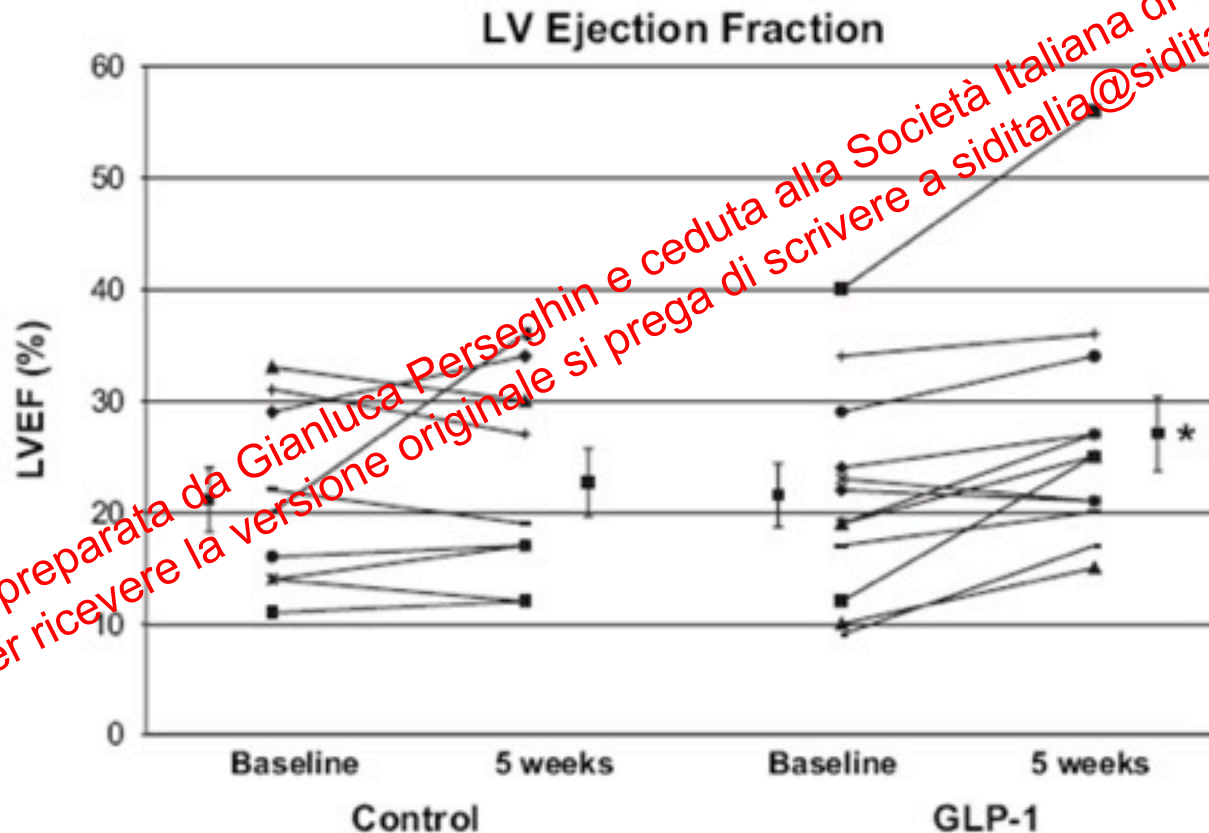
PBS



Exenatide

Myocardial effects of GLP1

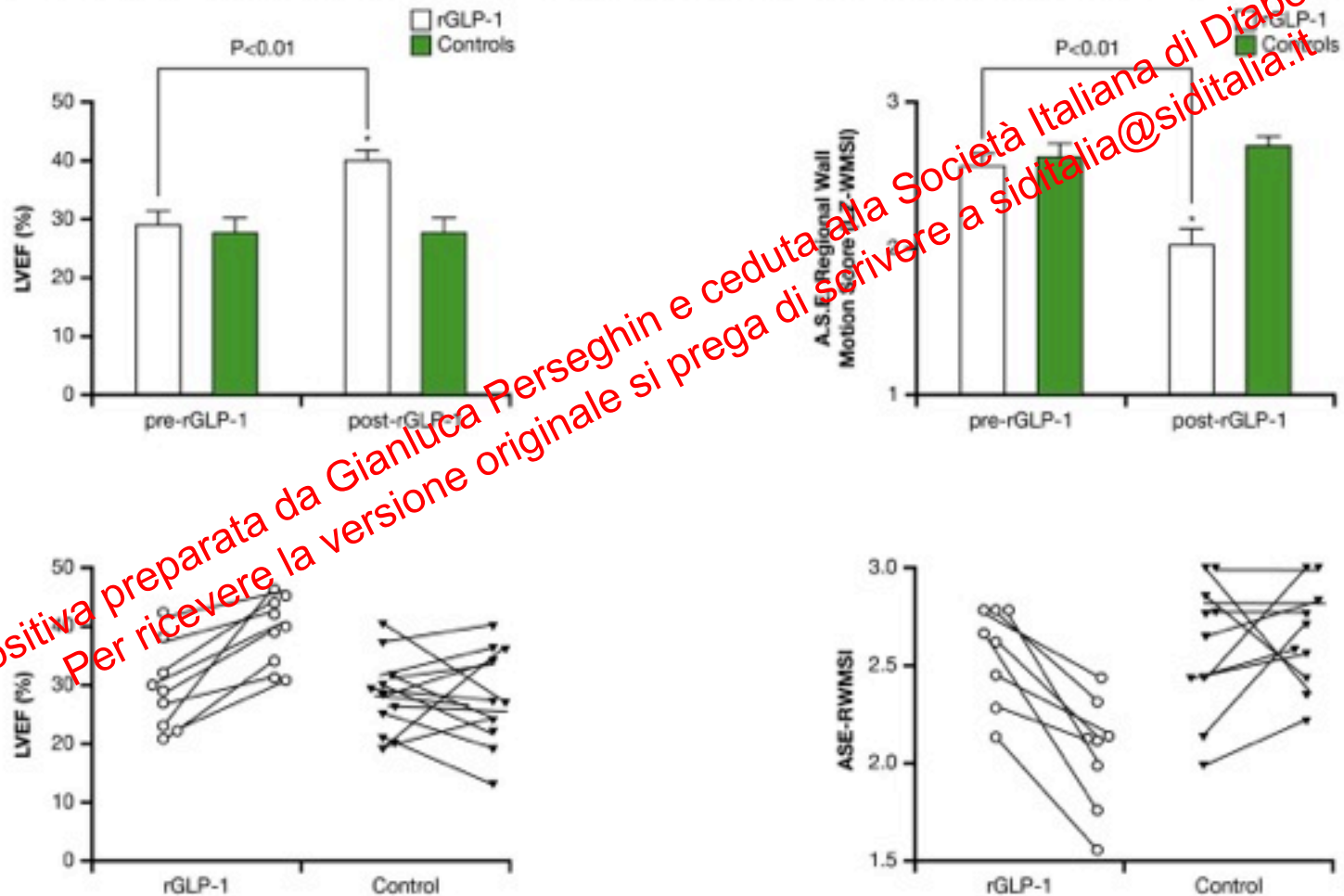
Non-diabetic patients with chronic heart failure
Effects of continuous subcutaneous GLP1 infusion



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Myocardial effects of GLP1

- Patients with MI and PTCA; effect of 72h human GLP-1 infusion



Final infarct size and short-term duration of ischemia

Exenatide i.v 15 min before procedure and for 6 hours

290

Circ Cardiovasc Interv

April 2012

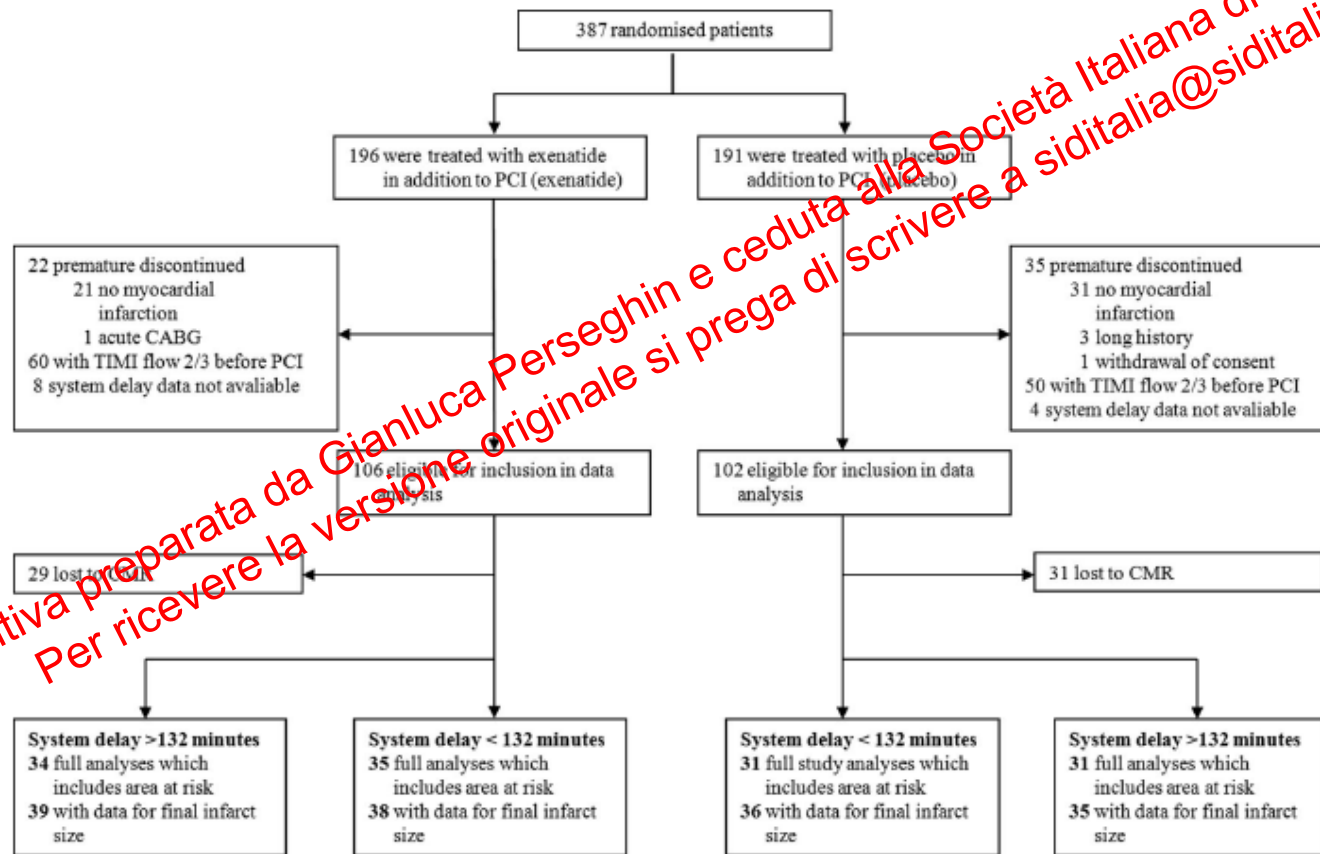
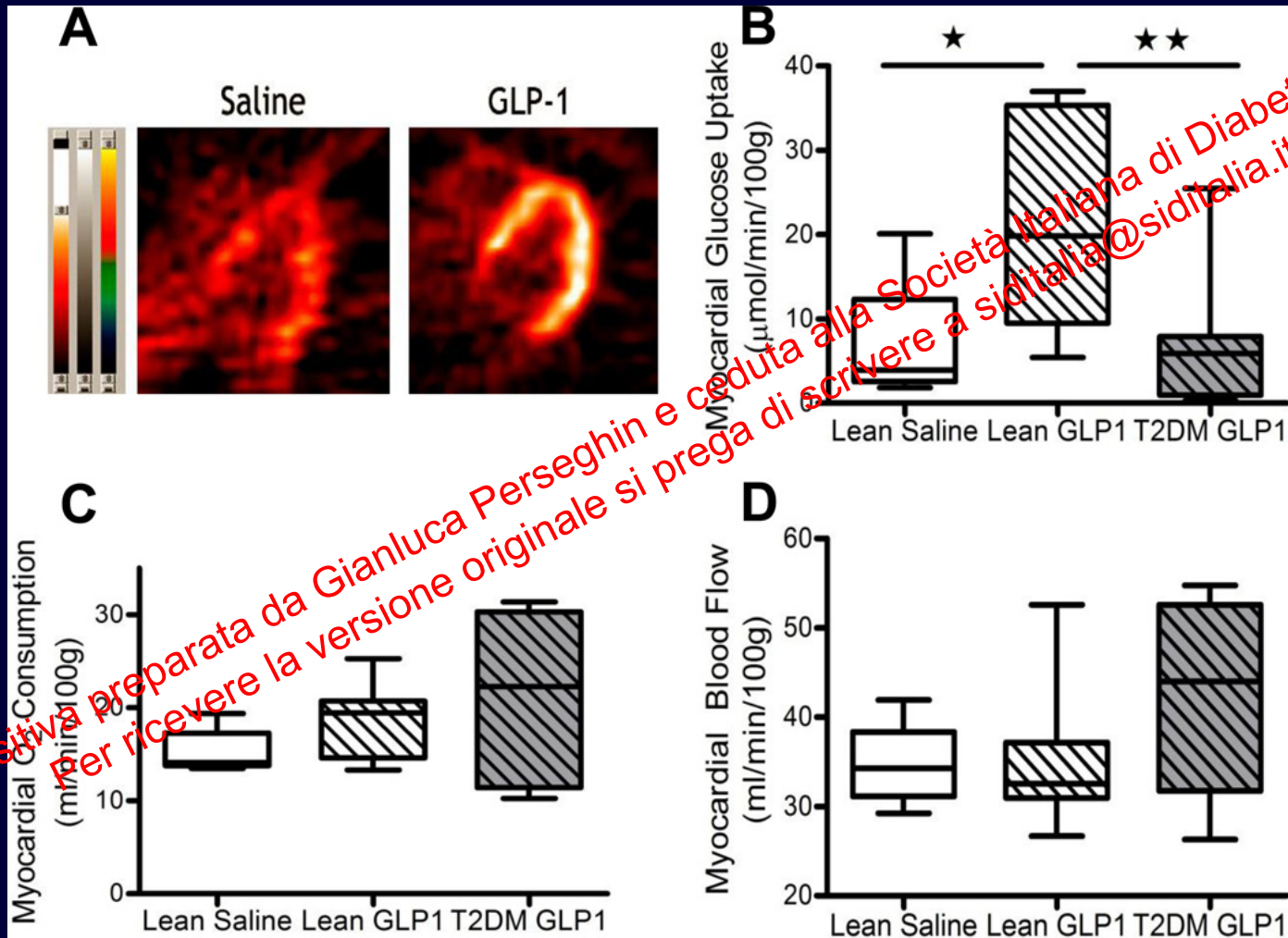


Figure 1. Trial profile. CABG indicates coronary artery bypass graft operation; CMR, cardiac magnetic resonance; PCI, percutaneous coronary intervention; and TIMI, Thrombolysis in Myocardial Infarction.

GLP1 and cardiac glucose metabolism



Moberly SP et al, Basic Res. Cardiol, 2013

Conclusioni

- IL GLP-1 svolge importanti effetti cardiovascolari dimostrati sia in modelli sperimentali sia nell'uomo
- Gli effetti sui meccanismi patogenetici dell'ATS possono essere molteplici e a diversi livelli
- I GLP-1RA possono inoltre modulare il metabolismo e la funzione del miocardio migliorando direttamente (recettoriale) e forse indirettamente (altro recettore ?) l'omeostasi energetica dell'organo