

Intra-abdominal obesity, metabolic risk factors and CHD



Abdominal obesity

Atherogenic dyslipidemia

↑ Triglycerides
↓ HDL-cholesterol
↓ Cholesterol/HDL- ratio
↑ apo B
Small, dense LDL and HDL
Postprandial hyperlipidemia

Insulin resistance

Insulin resistance
Hyperinsulinemia
Hyperglycemia
Type 2 diabetes

Thrombotic state

↑ PAI-1
↑ Fibrinogen

Inflammatory state

↑ CRP
↑ Cytokines

Metabolic risk factors

Inflammation

Lipid core

Thin fibrous cap

CORONARY ATHEROSCLEROSIS
UNSTABLE PLAQUE

↑ risk of acute
coronary syndrome

Adapted from Despres, 2004

NHLBI Obesity Education Initiative

The Practical Guide

Identification,
Evaluation,
and Treatment
of Overweight and
Obesity in Adults

W eight loss drugs approved by the FDA for long-term use may be useful as an adjunct to diet and physical activity for patients with a BMI ≥ 30 and without concomitant obesity-related risk factors or diseases. Drug therapy may also be useful for patients with a BMI ≥ 27 who also have concomitant obesity-related risk factors or diseases.



NHS
*National Institute for
 Health and Clinical Excellence*

Obesity
**guidance on the prevention,
 identification, assessment and
 management of overweight and obesity
 in adults and children**

BMI classification	Waist circumference			Comorbidities present
	Low	High	Very high	
Overweight				
Obesity I				
Obesity II				
Obesity III				

General advice on healthy weight and lifestyle
 Diet and physical activity
 Diet and physical activity; consider drugs
 Diet and physical activity; consider drugs; consider surgery

 2006

LiGIO'99

II.E.4.5. Terapia farmacologica

- I farmaci per la perdita di peso approvati dalla FDA (in Italia dal Ministero della Sanità) possono essere usati nell'ambito di un programma integrato, che include la terapia dietetica e l'attività fisica in soggetti con $BMI \geq 30$ senza fattori di rischio o malattie correlate all'Obesità, e in soggetti con $BMI \geq 27$ e fattori di rischio o malattie correlate all'Obesità.
- I farmaci per la perdita di peso non dovrebbero essere mai usati senza una contemporanea modifica dello stile di vita.
- La valutazione continua della sicurezza e della efficacia della terapia farmacologica è necessaria. Se il farmaco si rivela efficace nell'aiutare il soggetto a perdere e/o a mantenere la perdita di peso e se non si manifestano effetti avversi, il suo uso può essere continuato. Diversamente, il suo uso dovrebbe essere sospeso.



1999

OBESITÀ, SINDROME PLURIMETABOLICA
E RISCHIO CARDIOVASCOLARE:
CONSENSUS SULL'INQUADRAMENTO
DIAGNOSTICO-TERAPEUTICO

11. 4. 4. Nei pazienti con IMC compatibile con una condizione di **obesità lieve o moderata** la terapia farmacologica potrebbe avere uno spazio nell'ambito di un programma terapeutico integrato.
11. 4. 5. In questi pazienti, gli obiettivi dell'associazione del farmaco sarebbero:
- Riduzione dei fattori di rischio
 - Miglioramento della patologia associata
 - Facilitare il mantenimento del peso dopo una fase di calo ponderale.



2003

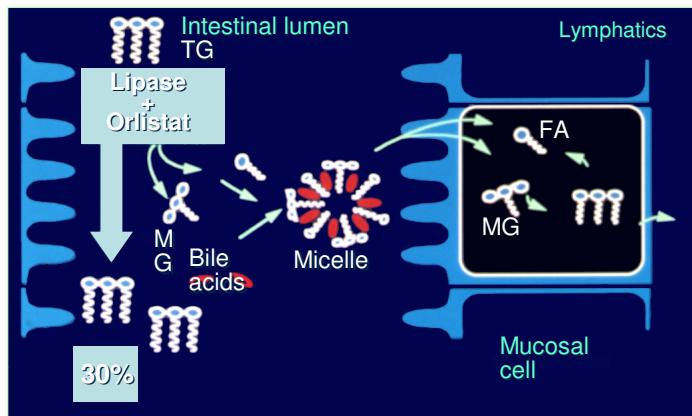
OBESITÀ, SINDROME PLURIMETABOLICA
E RISCHIO CARDIOVASCOLARE:
CONSENSUS SULL'INQUADRAMENTO
DIAGNOSTICO-TERAPEUTICO

11. 4. 6. Nei pazienti con IMC compatibile con una condizione di **obesità grave**, la terapia farmacologica potrebbe avere uno spazio nell'ambito di un programma terapeutico integrato.
11. 4. 7. In questi pazienti, gli obiettivi dell'associazione del farmaco sarebbero:
- Favorire la compliance alla dieta
 - Determinare un effetto "antabuse" verso alcune componenti della dieta
 - Facilitare un iniziale calo ponderale che motivi il paziente a proseguire il trattamento
 - Facilitare il mantenimento del peso dopo una fase di calo ponderale.

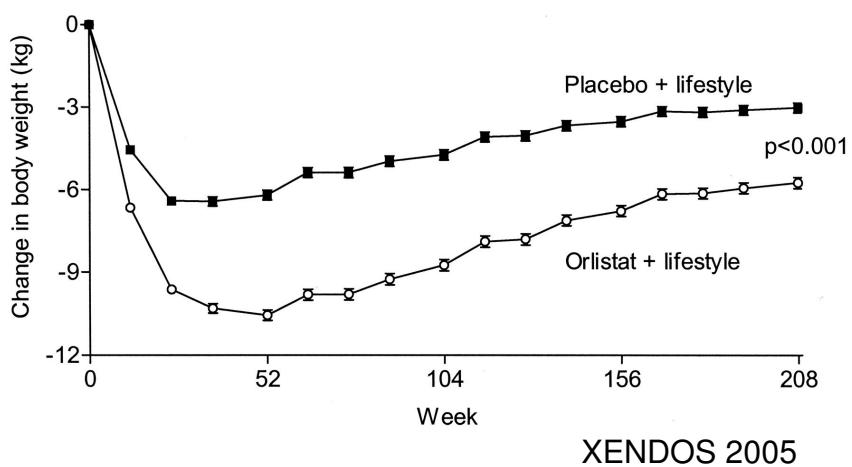


2003

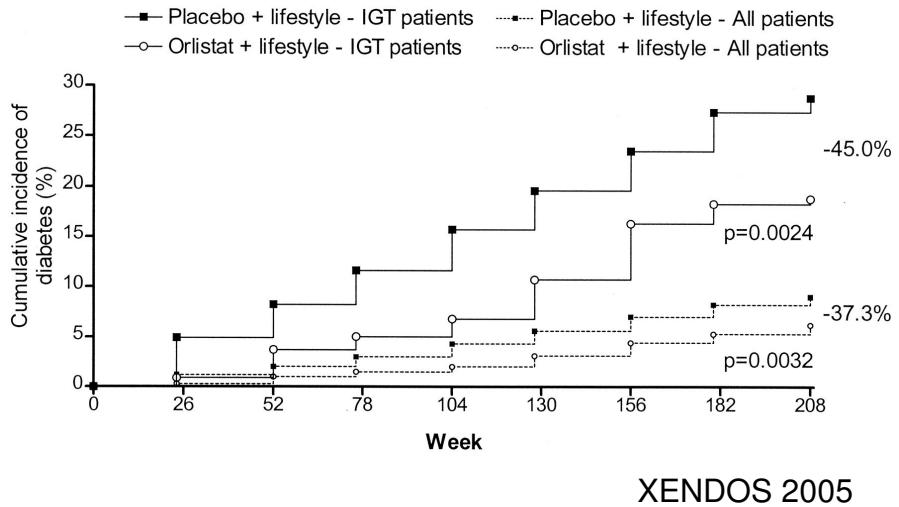
Orlistat



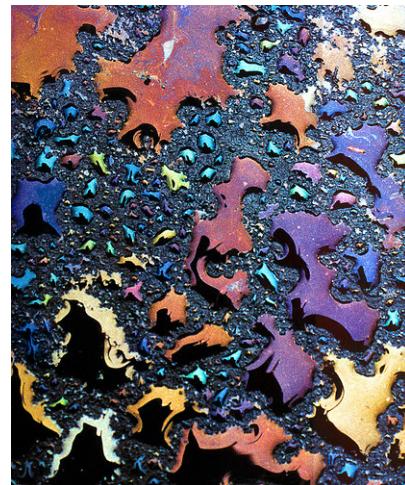
DiabetesCare



XENDOS 2005

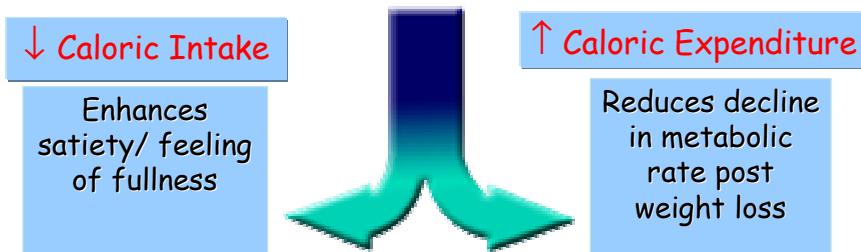


Oil spotting...

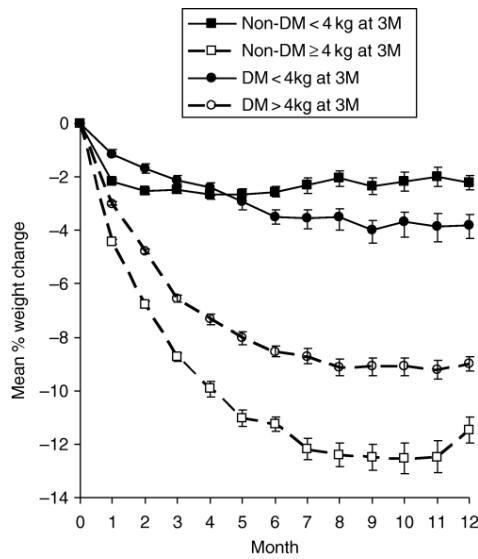


Sibutramine Mode of Action

- Centrally acting weight loss agent
- Serotonin and norepinephrine reuptake inhibitor



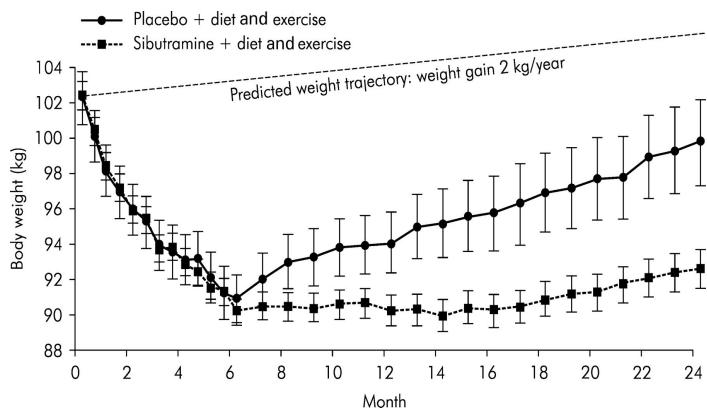
Mean percentage weight change over 12 months achieved by non-diabetic (DM) and DM patients according to achievement of 4kg weight loss target at month 3 (3M).



Finer, N. et al, 2006

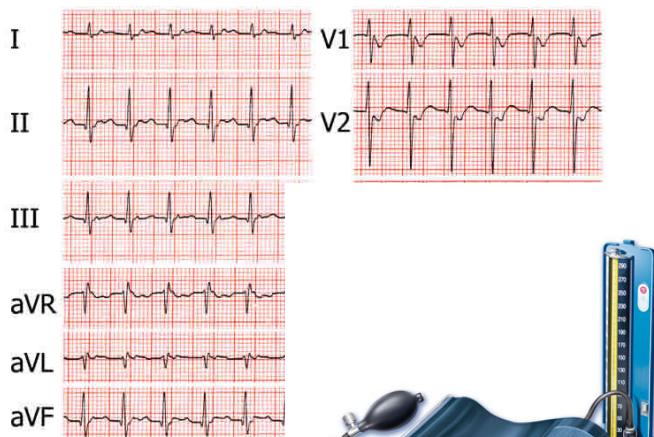
Weight loss and maintenance in the STORM trial.

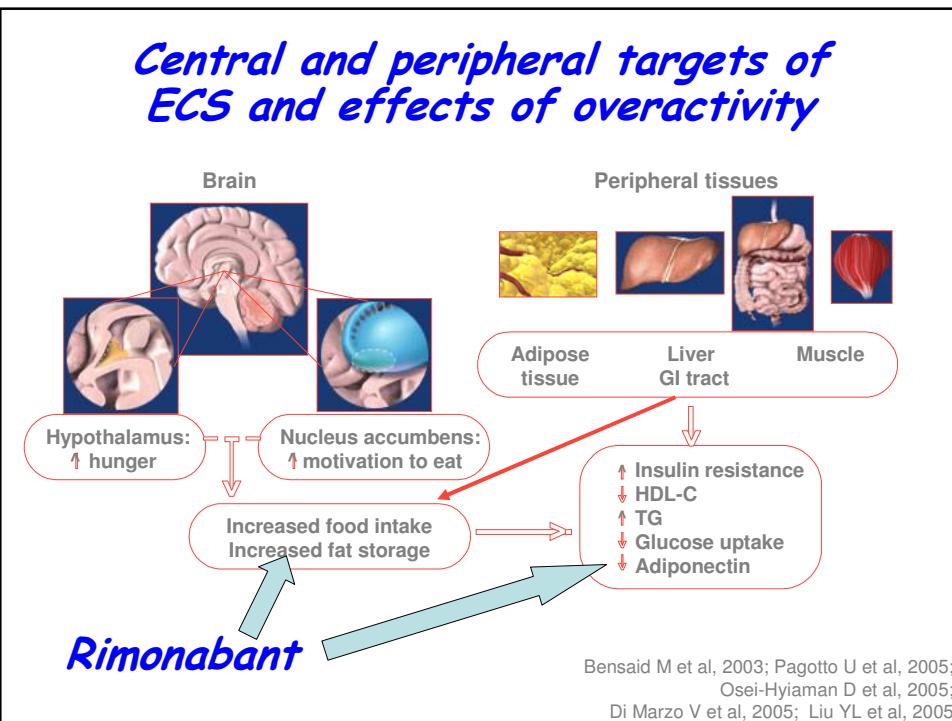
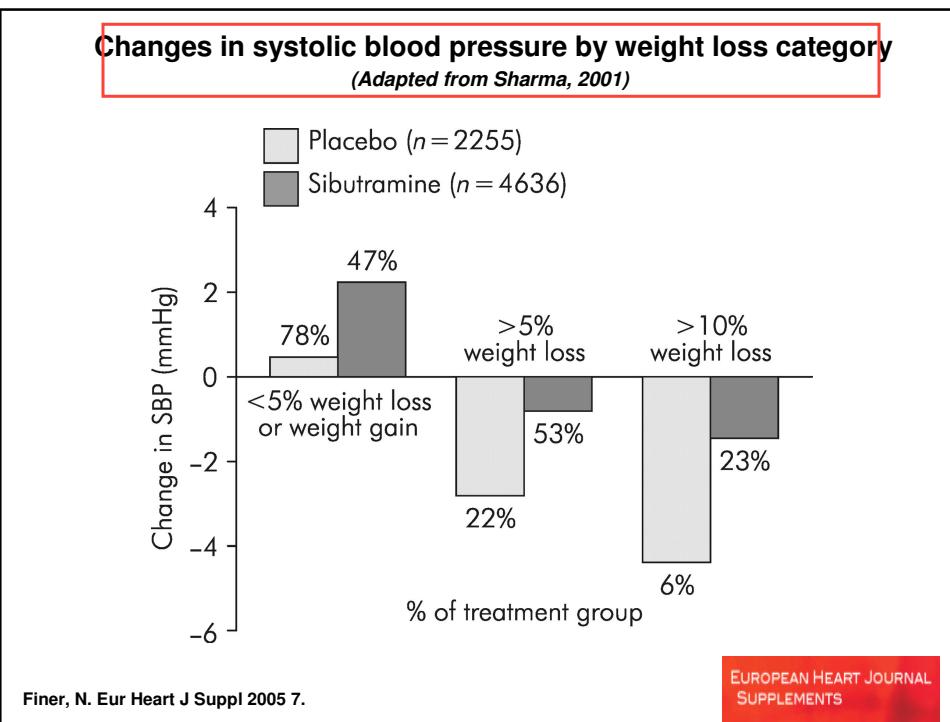
(Adapted from James et al.)

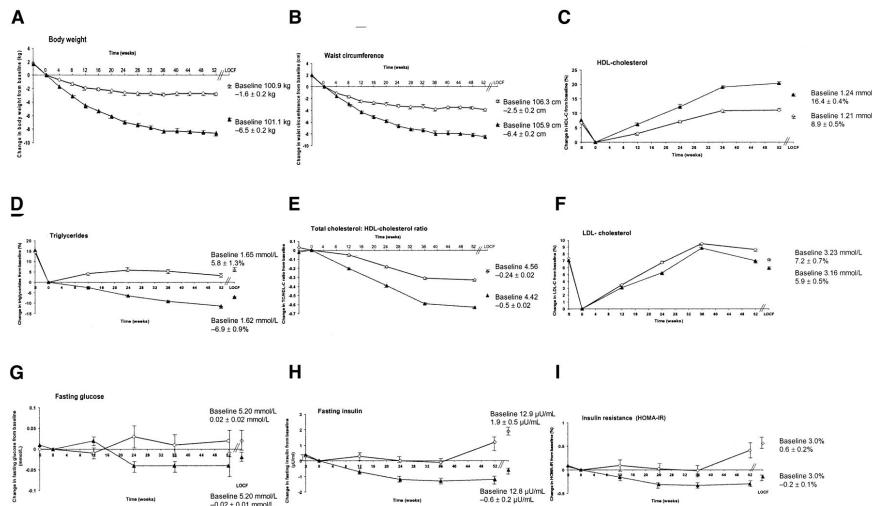


Finer, N. Eur Heart J Suppl 2005 7:L32-38L

EUROPEAN HEART JOURNAL
SUPPLEMENTS

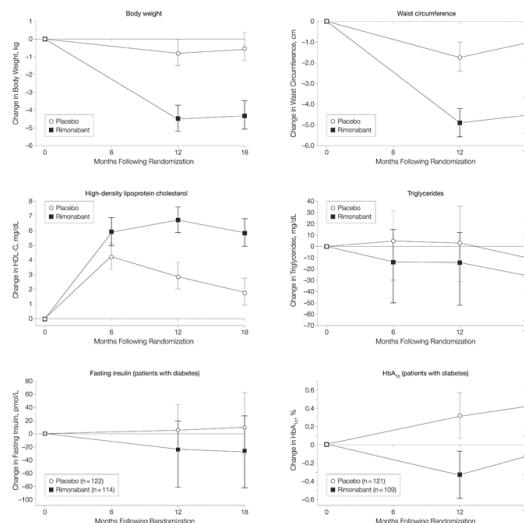






RIO combi, 2008

Effects of Rimonabant on Body Weight, Waist Circumference, and Levels of High-Density Lipoprotein Cholesterol (HDL-C), Triglycerides, Fasting Insulin, and Glycated Hemoglobin (HbA1c)



Nissen, S. E. et al. JAMA 2008;299:1547-1560.

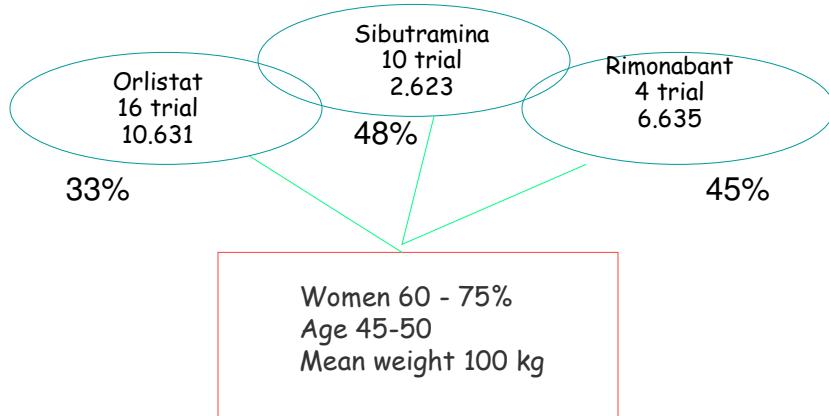
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JAMA

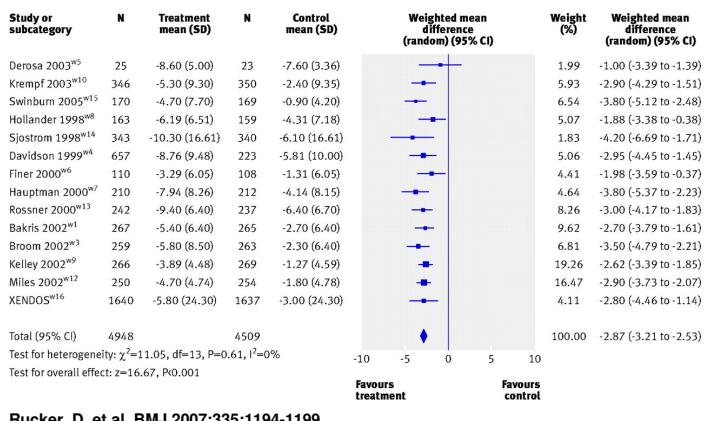


BMJ medical publication of the year

**Long term pharmacotherapy for obesity and overweight:
updated meta-analysis** Diana Rucker, Raj Padwal, Stephanie K Li,
Cintia Curioni, David C W Lau



Placebo subtracted weight reduction (kg) with orlistat

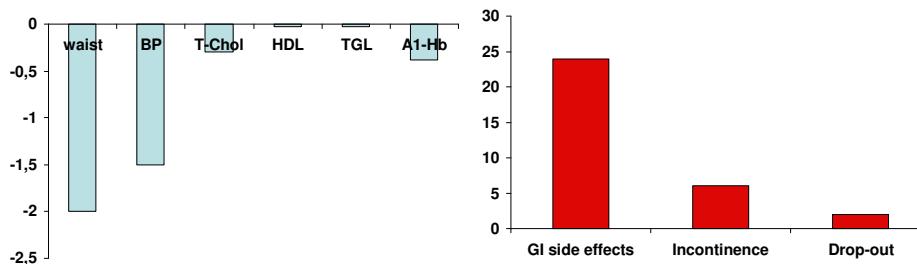


Rucker, D. et al. BMJ 2007;335:1194-1199

BMJ

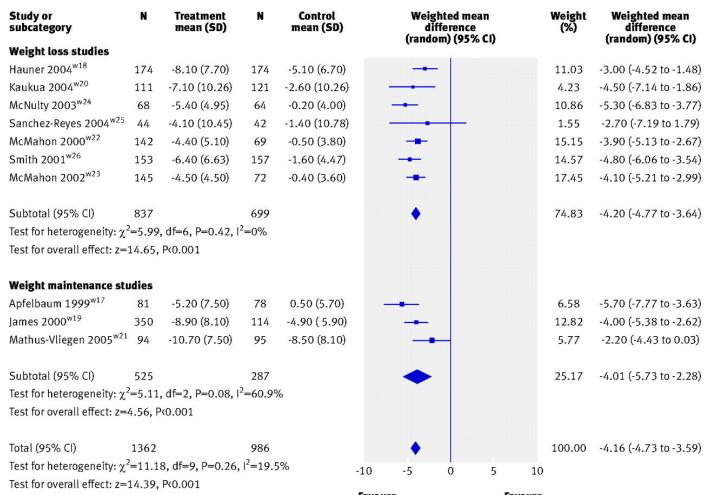
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BMJ



Orlistat

Placebo subtracted weight reduction (kg) with sibutramine

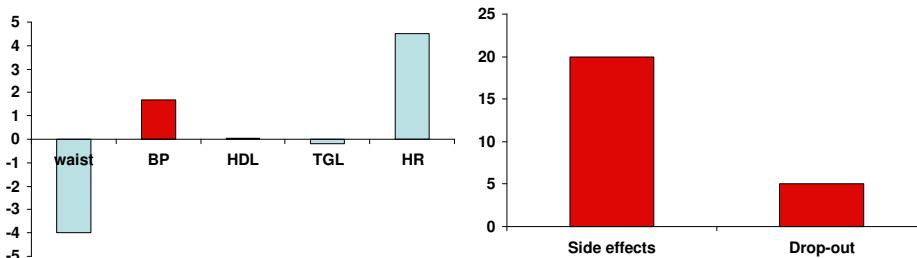


Rucker, D. et al. BMJ 2007;335:1194-1199

BMJ

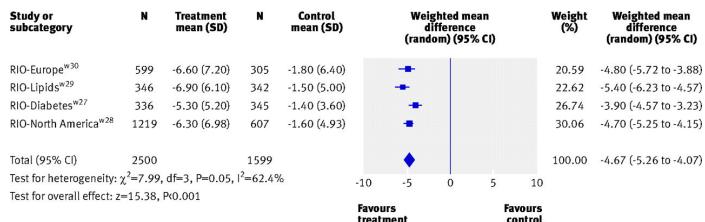
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BMJ



Sibutramine

Placebo subtracted weight reduction (kg) with rimonabant

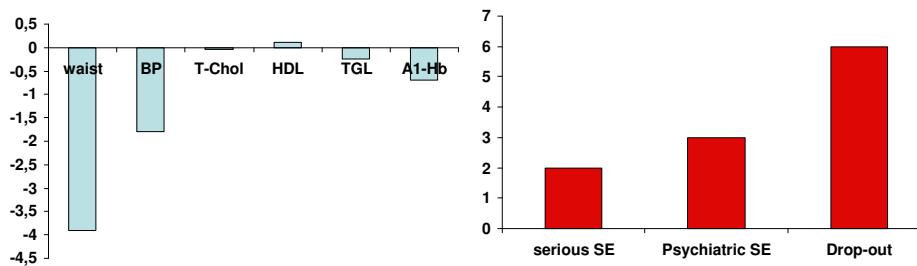


Rucker, D. et al. BMJ 2007;335:1194-1199

BMJ

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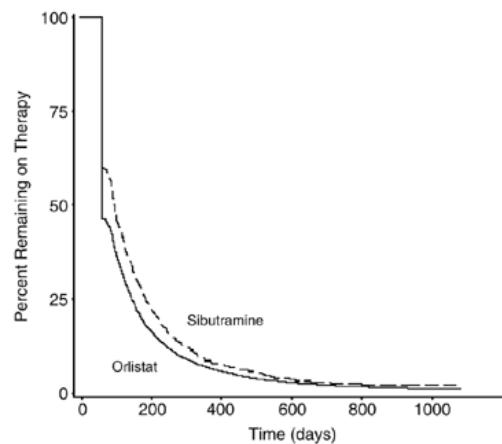
Rimonabant

Aspetti controversi relativi all'uso dei farmaci nella terapia dell'obesità

- Tempistica e durata del trattamento
- Selezione dei pazienti
- Ricerca dei "responders"
- Parametri di successo terapeutico
- Costo/beneficio



Long-term persistence



R Padwal, 2007

THE LANCET

"Irrespective of which drug is initially selected, treatment should be discontinued if clinically significant weight loss (ie, at least 5-10% of initial bodyweight or improvement in major obesity-related comorbidity) does not occur within the first 3-6 months"

R Padwal, 2007

Original Paper

Annals of
**Nutrition &
Metabolism**

Ann Nutr Metab 2007;51:75-81
DOI: 10.1159/000100824

Received: January 9, 2006
Accepted: August 8, 2006
Published online: March 15, 2007

Weight Loss and Quality of Life Improvement in Obese Subjects Treated with Sibutramine: A Double-Blind Randomized Multicenter Study

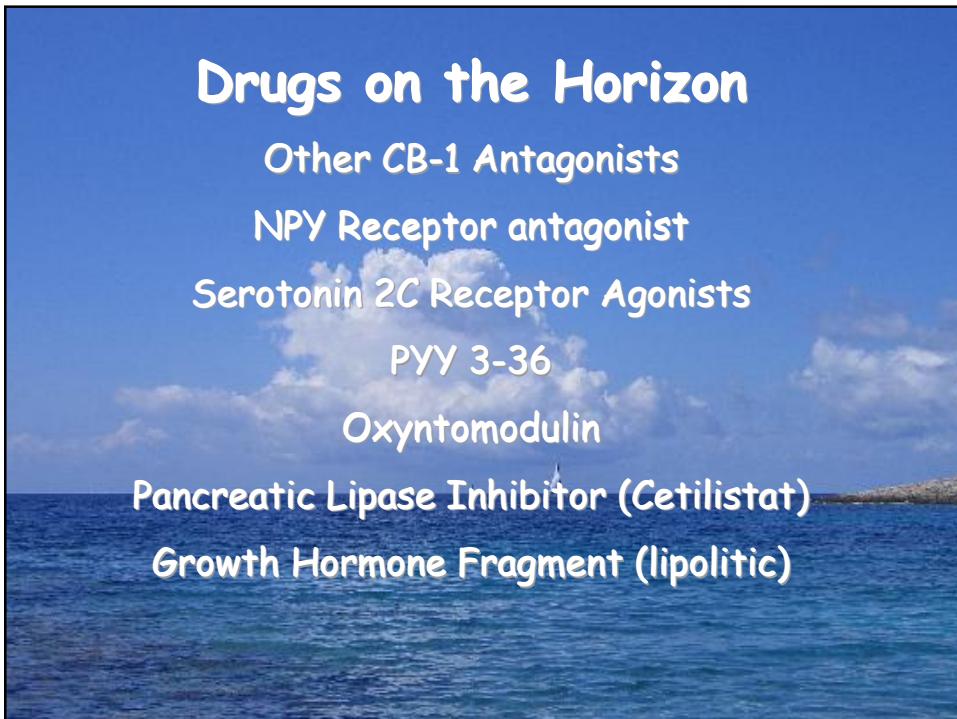
V. Di Francesco^a T. Sacco^b M. Zamboni^a L. Bissoli^a E. Zoico^a G. Mazzali^a
A. Minniti^a T. Salanitri^c F. Cancelli^c O. Bosello^a
for the Gruppo Italiano Studio Sibutramina



3-4 caffè!

20-33% della mia pensione..

- ✓ Orlistat (120 mg x 3) € 3,50/dì
- ✓ Sibutramina (10 mg x 1) € 2,75/dì
- ✓ Rimonabant (20 mg x 1) € 4,10/dì





Weight loss is the primary endpoint. Demonstration of a clinically significant degree of weight loss of at least 10% of baseline weight, which is also at least 5% greater than that associated with placebo, is considered to be a valid primary efficacy criterion in clinical trials evaluating new anti-obesity drugs.



*National Institute for
Health and Clinical Excellence*

The decision to start drug treatment, and the choice of drug, should be made after discussing with the patient the potential benefits and limitations, including the mode of action, adverse effects and monitoring requirements and their potential impact on the patient's motivation. When drug treatment is prescribed, arrangements should be made for appropriate health professionals to offer information, support and counselling on additional diet, physical activity and behavioural strategies. Information about patient support programmes should also be provided.



2006



Grazie per l'attenzione!