Next Generation Bariatric Metabolic Surgery - An integrated future

Where is Pharma Heading?

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IFSO, Melbourne, September 2024



In accordance with «EACCME criteria for the Accreditation of Live Educational Events», please disclose whether you have or not any conflict of interest with the companies:

[X] I have the following potential conflict(s) of interest to report:

- Receipt of honoraria or consultation fees: Honoraria from Novo Nordisk, iNova
- Other support : Royalties from the sale of Contrave ™

- Currently available drugs
- Drugs in late development
- The developing interest in preserving muscle/ building
- Combination surgery and drug therapy

Seminar

Obesity in adults

Ildiko Lingvay, Ricardo V Cohen, Carel W le Roux, Priya Sumithran

www.thelancet.com Published online August 16, 2024



- Older drugs
 - Phentermine,
 - Orlistat,

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 - Phentermine plus topiramate,
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 - Liraglutide,
- 4-10% placebo subtracted total body weight loss
- Some issues with tolerability

- New drugs
 - Semaglutide [GLF
 - Tirzepatide

[GLP-1 R], [GLP-1 R + GIP R],

- New drugs
 - Semaglutide [GLP-1 R],
 - Tirzepatide [GLP-1 R + GIP R],
- 12-18% placebo subtracted total body weight loss
- Significant other health benefits
 - HbA1c, MACE, apnoea,

- New drugs
 - Semaglutide [GLP-1 R],
 - Tirzepatide [GLP-1 R + GIP R],
- 12-18% placebo subtracted total body weight loss
- Significant other health benefits
 - HbA1c, MACE, apnoea,
- Some issues with tolerability / anaesthesia*
 - Nausea, vomiting, gastroparesis

- Newer drugs
 - Setmelanotide

[MC4 R]

- Used for rare genetic forms of obesity
- Substantial weight loss

Obesity Pharmacotherapies in Development

• Single/Multi-receptor agonists

 Orforglipron 	[oral GLP-1]	15%+
 Retruatide 	[GLP-1 R + GIP R + Glucagon R]	24%+
 Survotide 	[GLP-1R+GlucagonR]	19%+
 CagriSema 	[GLP-1 R + Amylin R]	16%+ (28%?)

Obesity Pharmacotherapies in Development

- Over 120 new agents in development
- Much more than Eli Lilly/ Novo Nordisk
- Other targets
 - Amylin
 - Activin/Myostatin

Role of Muscle

- Quality of life
- Energy Expenditure
 - Muscle, even resting, consumes significant energy,
 - Decreased energy expenditure can limit voluntary weight loss,
 - Loss of lean mass is a part of most weight loss,
 - Usually 1/5th of total loss is lean mass,
 - Unclear effects of GLP-1 R agonists on muscle mass
 - However, no reduction in EE with weight loss

Myostatin



No Myostatin



No Myostatin



Obesity Pharmacotherapies in Development

- Over 120 new agents in development
- Much more than Eli Lilly/ Novo Nordisk
- Other targets
 - Amylin
 - Activin/Myostatin
 - Urocortin
 - Apelin
 - All proposed to be muscle building or preserving.

30 % weight loss is possible with pharmacotherapy

- Pharmacotherapy tried before surgery for many patients
- More efficient pre-surgical weight loss if needed
- Better options if there is insufficient weight loss after surgery
- In combination, potential to bring weight down to 20-25 BMI?
- No understanding of why some patients respond to any particular drug
- No idea what will work best in combination
- Current drug costs \$5,500/year VS \$25,000

Thank you.