

Anti-Obesity Pharmacotherapy

Jessica Bartfield, MD

Diplomate of ABOM & NBPNS

Asst. Prof Dept of Surgery

Wake Forest Baptist Medical Center

Learning Objectives

Learning Objective(s) addressed in this presentation:

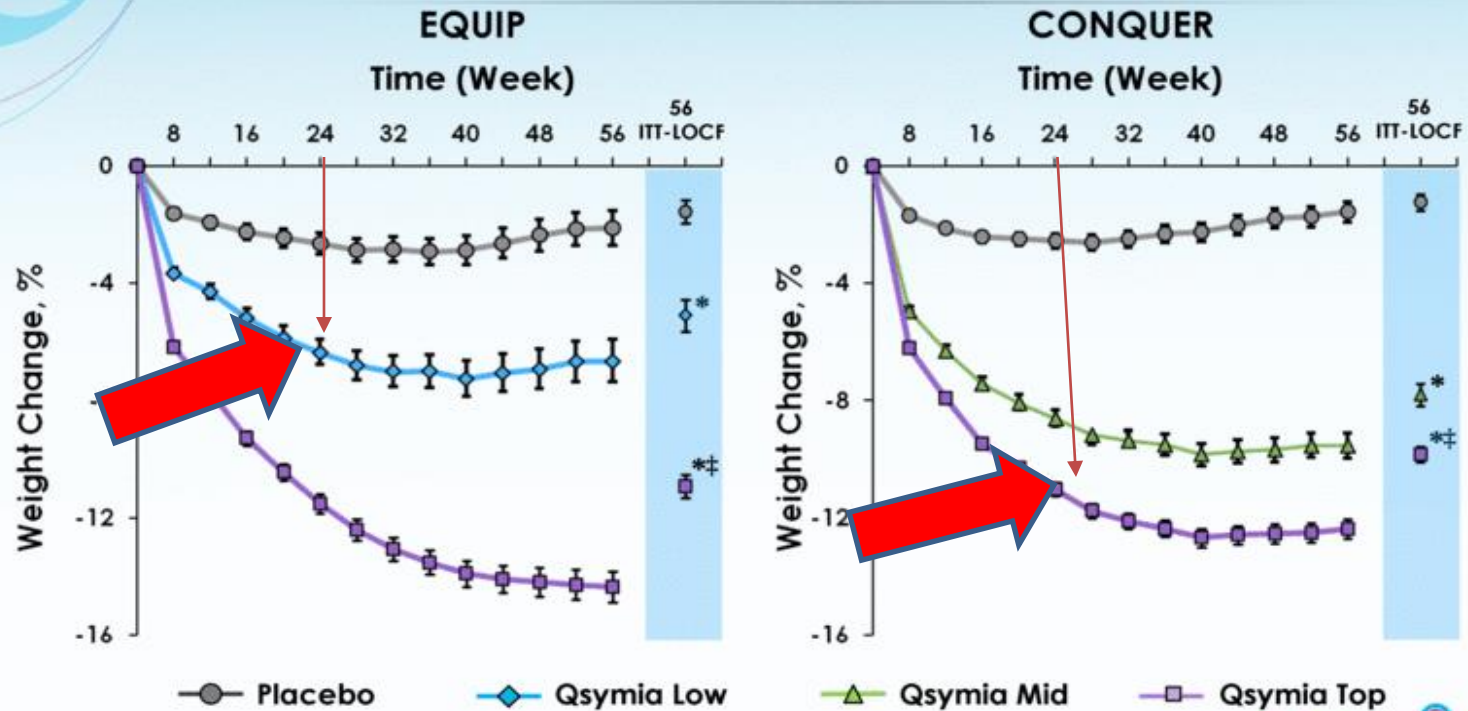
1. Understand the mechanism of action of FDA approved anti-obesity medications
2. Describe the average weight loss effects vs. duration of time for FDA approved anti-obesity medications
3. Recognize the most common side effects of FDA approved anti-obesity medications
4. Identify any contraindications for use

FDA approved anti-obesity medications

Phentermine/Topamax (Qsymia-2012)

- Increased norepinephrine through phentermine + GABA (gamma-aminobutyric acid) influences in brain(?)
- taste inhibition from carbonic anhydrase of Topamax(?)¹
- appetite suppression
- chronic weight management
- average weight loss 15-19 lbs. at one year
 - 50-54% achieved >10% wt. loss at 2yr
 - 9-15% achieved >20% wt. loss at 2

Pivotal 1-Year Studies: Weight Loss Over Time (Observed Data)



All observed data; *p<0.0001 vs placebo; †p<0.0001 vs. Qsymia Mid or Low



FDA approved anti-obesity medications

Phentermine/Topamax

- Common side effects:
 - a. dry mouth
 - b. insomnia
 - c. paresthesia
 - d. dizziness
 - e. taste changes



FDA approved anti-obesity medications

Phentermine/Topamax

-Contraindications

- a. **Category X for pregnancy**
- b. glaucoma
- c. hyperthyroidism

-Dosages

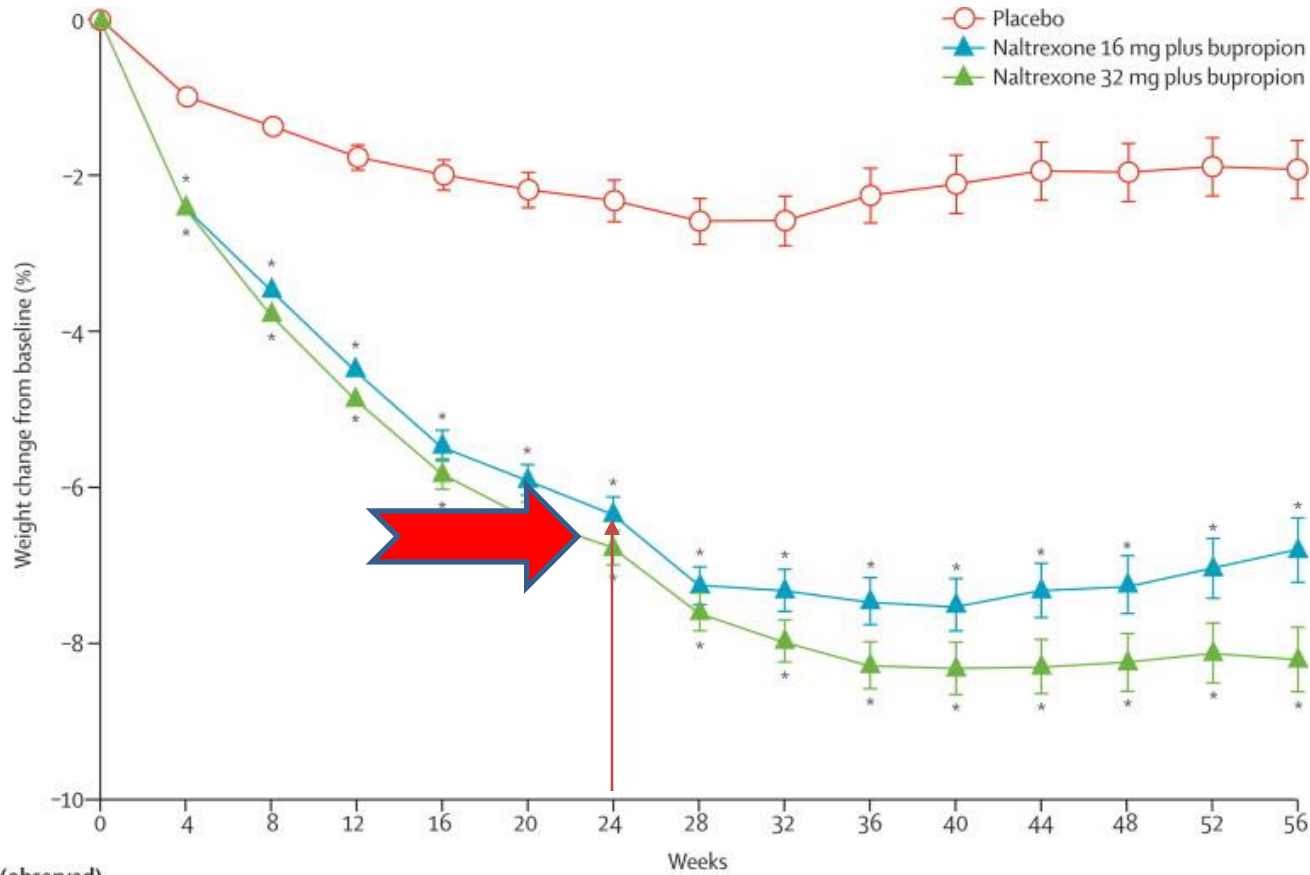
- a. 2 week low dose 3.75 mg/23 mg
- b. standard dose 7.5mg/46 mg
- c. titration 11.25mg/69 mg
- d. high dose 15 mg/92 mg

FDA approved anti-obesity medications

Naltrexone/Bupropion (Contrave-2014)

- Increases levels of dopamine and norepinephrine + blocks mu opioid receptor within the brain
- appetite suppressant + decreased reward(?)
- chronic weight loss treatment
- average weight loss 4.8% at one year
 - 41.5% lost >10% at 1 year in BMOD
 - 29.1% lost >15% at 1 year in BMOD³

Contrave



Number of participants by visit (observed)

| | 0 | 4 | 8 | 12 | 16 | 20 | 24 | 28 | 32 | 36 | 40 | 44 | 48 | 52 | 56 |
|---------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Placebo | 507 | 463 | 420 | 394 | 365 | 353 | 327 | 318 | 308 | 302 | 296 | 291 | 289 | 287 | 277 |
| Naltrexone 16 mg plus bupropion | 467 | 410 | 373 | 351 | 346 | 341 | 311 | 311 | 302 | 297 | 300 | 284 | 283 | 273 | 273 |
| Naltrexone 32 mg plus bupropion | 467 | 411 | 391 | 372 | 365 | 361 | 343 | 327 | 321 | 316 | 311 | 305 | 298 | 284 | 284 |

FDA approved anti-obesity medications

Naltrexone/Bupropion

-Common Side effects:

- a. Nausea
- b. constipation
- c. headache
- d. vomiting
- e. dizziness
- f. Insomnia
- g. dry mouth

FDA approved anti-obesity medications

Naltrexone/Bupropion

-Contraindications

- a. seizure disorder or risk of seizure
- b. uncontrolled hypertension
- c. bulimia
- d. ESRD
- f. chronic opioid use



-Dosage

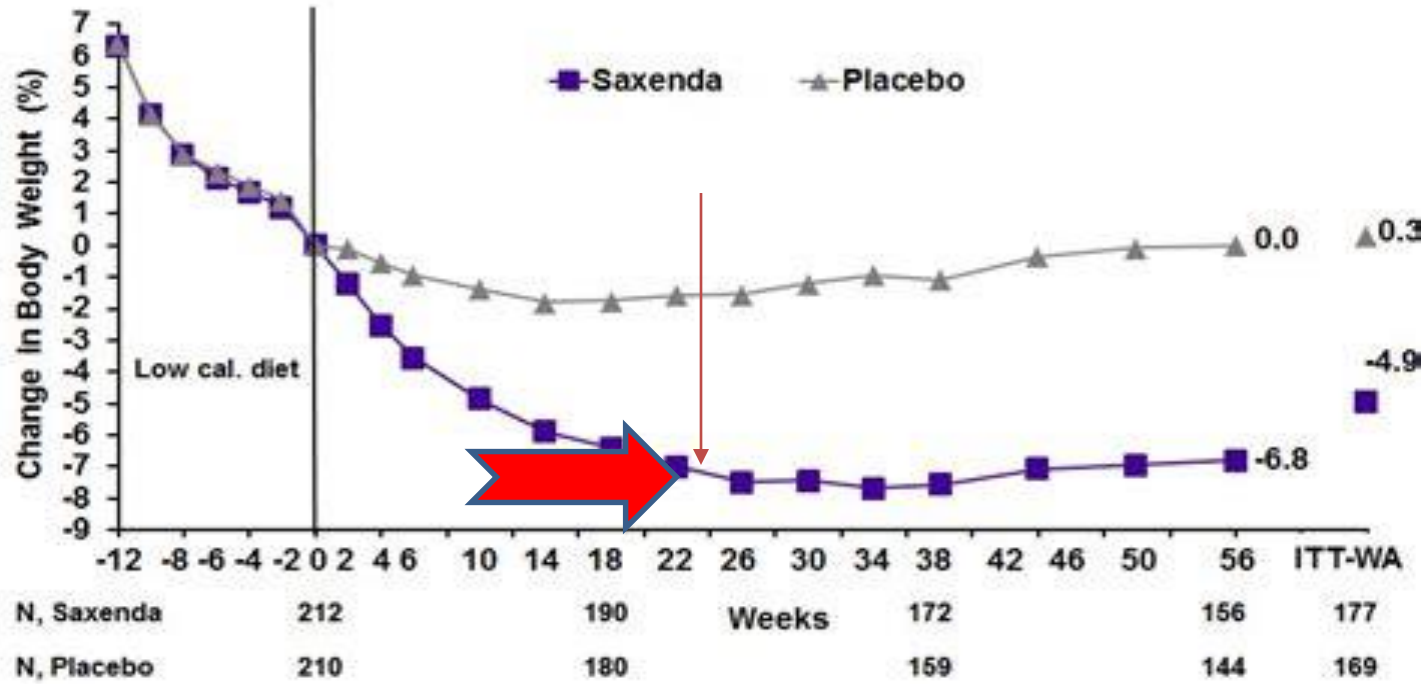
extended release 8/90mg 2 tabs BID

FDA approved anti-obesity medications

Liraglutide 3mg (Saxenda- 2014)

- Glucagon-like peptide-1 receptor agonist that stimulates glucose dependent insulin release, slows gastric emptying
- appetite suppression and increased satiety
- Liraglutide 1.8mg (Victoza) FDA approved for type 2 diabetes
- Chronic obesity treatment
- Average weight loss 5.8kg at one year
 - a. 33% lost at least 10% of body weight⁴

Saxenda



Observed values for patients on study drug completing each scheduled visit, and ITT with weighted average (ITT-WA)

FDA approved anti-obesity medications

Liraglutide

-Common Side effects

- a. nausea
- b. vomiting
- c. diarrhea/constipation
- d. hypoglycemia
- e. pancreatitis
- f. gallbladder disease
- g. suicidality (?)
- h. increases in heart rate (?)

FDA approved anti-obesity medications

Liraglutide

-Contraindications

- a. Medullary thyroid cancer history
- b. multiple endocrine neoplasia type 2

-Dosage 3.0mg injected SC once daily



FDA approved weight loss medications

Systemic review and meta-analysis: 28 RCTs

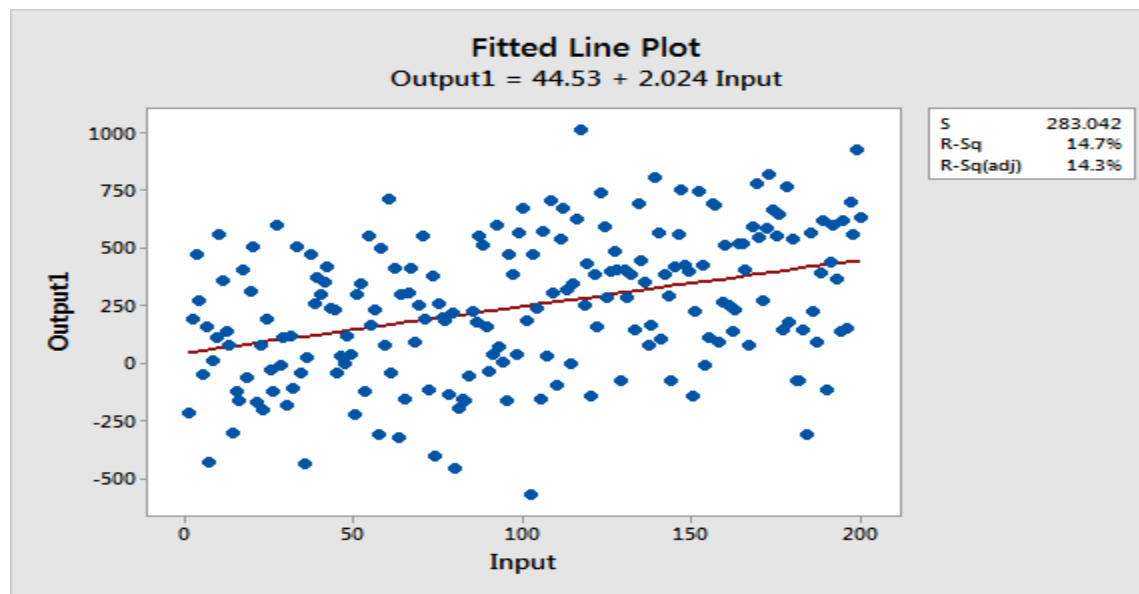
| Medication | Weight loss Efficacy Rank | Adverse Event Rank |
|------------------------|---------------------------|--------------------|
| Orlistat | 5 | 2- stool changes |
| Locaserin | 4 | 1- headache, dizzy |
| Phentermine/topiramate | 1 | 3-dry mouth |
| Naltrexone/bupropion | 3 | 4-nausea |
| Liraglutide 3mg | 2 | 5- GI symptoms |

All were associated with 5% weight loss at 52 weeks

FDA approved weight loss medications

Problems:

- High attrition
- Very little direct comparison studies
- High variability among studies
- High variability in results



FDA approved weight loss medications

Future Targets (?)

- Adipose tissue

 - Leptin receptor agonist

- Pancreatic hormones

 - PP (pancreatic polypeptide) analog

- Central neuropeptide Signaling

 - NPY (neuropeptide Y)

Goal: Effective, specific, individualized treatment

Two Final Considerations...

Medications that are FDA
approved for other
purposes

1. Metformin
2. Topamax
3. Wellbutrin
4. Zonisamide
5. Vyvanse
6. Jardiance
7. Victoza
8. Byetta

Medications that can
cause weight gain

1. Steroids
2. Insulin
3. Sulfonylureas
4. Antipsychotics
5. TCAs
6. Depo Provera
7. Beta Blockers
8. Anti-seizure
9. Neuropathy meds

References

1. Xiong GL, Gadde KM. Combination phentermine-topiramate for obesity treatment in primary care: a review. *Postgrad Med* 2014; 126:110-116.
2. Garvery WT, Ryan DH, Look M. Two-year sustained weight loss and metabolic benefits with controlled-release phentermine/topiramate in obese and overweight adults (SEQUEL): a randomized, placebo-controlled, phase 3 extension study. *Am J Clin Nutr* 2012;95:297-308.
3. Wadden TA, Foreyt JP, Foster GD, et al. Weight loss with naltrexone SR/bupropion SR combination therapy as an adjunct to behavior modification: The COR-BMOD Trial. *Obesity* 2011; 19(1): 110-120.
4. Pi-Sunyer X, Astrup A, Fujioka K, et al. A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. *N Engl J Med* 2015; 373(1): 11-22.
5. Khera R, Murad, MH, Chandar AK, Dulai PS, et al. Association of Pharmacological Treatments for Obesity with weight loss and adverse events. A systematic review and meta-analysis
6. Kim et al. *Clin Pharmacol Ther.*