Patient Case:
A 34-year-old overweight AA female presents to clinic for mental health follow up. The patient lost her insurance due to losing her job and was not on any medications for 2-3 months, however she is now enrolled in a patient assistance program. Before losing her insurance, she was on Zoloft 50mg daily for anxiety and depression. She continues to have increased crying spells, panic attacks, and difficulty getting out of bed despite increasing sertraline 100mg about one month ago. She also complains of sexual dysfunction with sertraline. She has a history of substance use disorder 10 years prior and wants to avoid taking benzodiazepines if possible. PHQ-9 score was a 17 prior to dosage increase, however, now the score is 14.

PMH:
Major Depressive Disorder with anxious distress
GERD
HTN

Labs:
eGFR: 119
Glucose: 64
BUN: 12
Scr: 0.76
Na: 141
K: 4.5

Vitals:
BP 161/89
HR 80
Tmax 98

Current medications:
Sertraline 100mg daily
Omeprazole 20mg daily
HCTZ 12.5mg daily

Questions

1. If you wanted to keep the patient on an SSRI, which agent in that class would you use to decrease or potentially eliminate sexual dysfunction?
    a. Trintellix (vortioxetine) is studied with less sexual dysfunction when compared to escitalopram but patient has anxiety and there is no evidence associated with using vortioxetine and anxiety (J Sex Med. 2015 Oct;12(10):2036-48. doi: 10.1111/jsm.12980. Epub 2015 Aug 31.)
        i. Trintellix inhibits the reuptake of serotonin; also has agonist activity at the 5-HT1A receptor and antagonist activity at the 5-HT3 receptor.
    b. If the adverse effects weren't an issue, it is recommended to increase to the max tolerated dose of the initial medication. The max dose of sertraline is 200mg/day (for general depression) and could be considered since patient had an improvement in PHQ-9. Another evidence-based first-line option would be citalopram and escitalopram, but we would also be concerned about sexual dysfunction in this particular patient.

2. If you decide you want to switch the patient to another agent, what are 3 potential treatment options (select a specific agent and justify your answer)?
    a. Venlafaxine
        i. In STAR*D, 25% of patients reached remission when switched from citalopram to venlafaxine. However, this may not be the best option in a patient with uncontrolled hypertension due to the norepinephrine activity.
    b. Mirtazapine
        i. In a study by Guelfi et al they found that mirtazapine compared to venlafaxine, resulted in a higher percentage of responders and remitters. A common adverse effect is weight gain so this may not be the best option in an overweight patient.
    c. Bupropion (the best option in my opinion)
        i. Based on study by Trivedi et al that bupropion and sertraline were comparably effective and superior to placebo in reducing depressive symptoms and did not differ on their effects on anxiety. Thus, switching to bupropion XL would be an option. Bupropion also has a decreased chance of sexual dysfunction compared to other agents and can decrease appetite leading to weight loss. In the STAR*D trial, patients with anxious depression had lower remission rates than patients with non-anxious depression. In patients with **anxious** depression, the highest remission rates were reached when patients were switched from citalopram to venlafaxine or bupropion compared to sertraline.

3. The patient has been on bupropion for 12 weeks and reports improvement in sexual dysfunction. The patient's anxiety has improved slightly but is not completely controlled. The depression symptoms have improved but have not reached remission. What are 3 potential treatment options for augmentation at this time?

    a) Mirtazapine
        i. Augmentation with mirtazapine is a possibility. However, a common adverse effect is weight gain so this may not be the best option in an overweight patient. Mirtazapine is a tetracyclic antidepressant that acts by antagonizing the

α2-autoreceptors and α2-heteroreceptors. Antagonism at these receptors block the inhibitory signals allowing for increased NE and serotonin release. It also blocks 5-HT2 which has been shown to increase antidepressant effects and 5-HT3 receptors which has been shown to help patients suffering from nausea and vomiting. It also blocks the H1 receptor, which is associated with weight gain and increase in appetite.

b) Lithium or triiodothyronine (T3)
    i. Augmentation with lithium can be a potential option. Of the patients reaching remission in step 3 of STAR*D, 14.5% reached remission when lithium was added to bupropion and only 9.1% reached remission when lithium was added to sertraline. Intolerance rate was higher in the bupropion plus lithium group vs the sertraline plus lithium group. When adding lithium, serious adverse effects need to be considered including tremors and serum levels need to be monitored. T3 is also an option for augmentation. In step 3 of STAR*D, 37.5% of patients reached remission with bupropion plus T3 vs 10% with sertraline plus T3.
c) Nutrients
    i. Augmentation with nutrients or light therapy. There is some evidence supporting nutrients such as omega-3 fatty acid and L-methylfolate.
d) Antipsychotics (the best option in my opinion)
    i. Augmentation with quetiapine, risperidone, aripiprazole, or brexpiprazole. There is evidence with risperidone as an augmenting agent with SSRIs. However, the evidence is limited for this case due to the fact that it has been studied as an augmentation agent with an SSRI and not bupropion. Quetiapine may be a good option for patients struggling with comorbid insomnia. Aripiprazole has been shown to be efficacious when added to initial therapy for patients with major depressive disorder with anxious features. Aripiprazole also has less metabolic adverse effects. It is also important to note that any antipsychotics can cause EPS, but the risk is lower with aripiprazole in comparison to other antipsychotics. Brexpiprazole is another option but may not be affordable for many patients.

4. The patient is still not in remission. She is now complaining of sleeping all day and eating more than usual despite bupropion. The patient takes 4-5 naps per day that last 30-60 minutes. The patient also states that she feels as though her mother does not want to speak to her anymore due to her excessive eating and weight gain. Which treatment option should be considered?
    i. If the patient is still not in remission, we should look for an atypical features specifier such as hyperphagia, hypersomnia, leaden paralysis, and pathological rejection sensitivity. Because this patient is exhibiting atypical features, a MOAI such as phenelzine or selegiline should be considered. Combination SSRI plus aripiprazole has also shown benefit in patients with atypical features.
    ii. If this patient did not have atypical features, consider switching to venlafaxine (if not previously tried) or a TCA such as nortriptyline.