Goal: To peruse low dose testosterone therapy with the concurrent use of a DHT blocker in order to attempt to limit dysphoria because of changes caused by DHT, while retaining the effects of testosterone.

I fully understand that one can not pick and choose what my hormone effects will be but I have significant concerns in three areas relating to the effects of DHT specifically. Because of my status as a non-binary person, and because many of the effects of DHT are irreversible, I would like to begin with this combination to attempt to limit some of these traits. If I do not get my desired results or if the DHT blocker is causing safety concerns I am more than willing to continue with a more traditional low dose approach.

<u>Testosterone is primarily responsible for</u>: deepening of the voice, masculine facial structure, male-pattern fat distribution, increased muscle mass, vaginal atrophy, emotional changes, thickening of the skin, acne, increased libido, also the possibility higher blood pressure, elevations in glucose and other negative health effects.

<u>DHT is primarily responsible for:</u> clitoromegaly (bottom growth), secondary hair growth (facial and body hair), triggering male pattern baldness, some aspect of libido (shown in cis men), and possibly has some effect on the thickening of vocal cords (some, but very little solid evidence of this)

The safety of possibly long term use of DHT blockers and any issues with taking testosterone with a DHT blocker in relation to masculinizing effects.

<u>Safety</u>: Although there is little evidence of the use of DHT blockers especially in cis women or transgender patients there have been some studies on the long term effects of the drug in use of hair loss.

5-alpha reductase inhibitors, such as finasteride and dutasteride, are becoming more commonly prescribed for women with hair loss. The limited number of studies indicate that 5ARIs are well-tolerated initially with no increased risk of malignancy or severe side effects; however, headache, gastrointestinal discomfort, and decreased libido are the most common side effects reported.

Currently, there is no direct link between 5ARI use and depression; however, several small studies have led depression to be listed as a side effect on the medication packaging.

Fortunately the effects are usually mild, with large studies suggesting the symptoms improve over time.

Hirshburg JM, Kelsey PA, Therrien CA, Gavino AC, Reichenberg JS. Adverse Effects and Safety of 5-alpha Reductase Inhibitors (Finasteride, Dutasteride): A Systematic Review. *J Clin Aesthet Dermatol.* 2016;9(7):56–62.

This study indicates that the long term use of a DHT blocker does have side effects but with proper monitoring they are manageable and seem to decrease with time. It is worth noting that finasteride and dutasteride are often used indefinitely to combat balding in cis men.

<u>Use of DHT blocker and Testosterone</u>: There is a common belief that using these two drugs in tandem would simply cancel out the effects.

Since [finasteride and dutasteride] block neither the production nor action of testosterone, their antiandrogen effect is less than that encountered with full blockade.

"Overview of Masculinizing Hormone Therapy | Transgender Care." *Ucsf.Edu*, 2019, transcare.ucsf.edu/guidelines/ Accessed 9 Aug. 2019.

The three areas in which I have concern about the effects of DHT causing dysphoria.

1) Body hair growth: This information is from an article that analyzes studies done on 5α -reductase deficiency. DHT is responsible for the initial development of follicles that are seen in secondary male hair characteristics such as face and body hair. This is also indicated in other literature.

[W]hile DHT is pushing scalp hair follicles to their doom, it is also stimulating facial hair follicles in the beard area to produce heavier, longer shafts. So if a trans guy takes finasteride to arrest the loss of scalp hair, he might also be stopping or slowing new facial hair growth.

americantransman. "Beards, Baldness and What's in Your Pants." *American Trans Man*, American Trans Man, 15 Apr. 2012, americantransman.com/2010/04/12/beards-baldness-and-whats-in-your-pants/. Accessed 9 Aug. 2019.

Finasteride can also be used to prevent male-pattern baldness in transgender men, as it only blocks dihydrotestosterone (DHT), not testosterone itself; however this will likely slow or decrease secondary hair growth...

"What Are Commonly Used Medications for Transition?" *TransLine: Transgender Medical Consultation Service*, 2019, transline.zendesk.com/hc/en-us/articles/229373208-What-are-commonly-used-medications-for-transition-. Accessed 9 Aug. 2019.

Clitoromegaly:My second area of concern is bottom growth (clitoromegaly). The typical trans male narrative includes the want for bottom growth and although I am looking for masclunization, I do not have much genial dysphoria or a want for my genitalia to resemble that of a male's. As a non-binary person I believe that changes in my genitals could cause more dysphoria than I currently have and would like to limit these effects if at all possible. This relates again back to the studies on 5α -reductase deficiency. As well as treatment options in order to stimulate more genital growth in men which shows that DHT plays a significant role in growth.

This role of DHT becomes evident in cases of the intersex condition 5α -reductase deficiency which is due to mutation of the gene for the Type 2 form of the enzyme. These individuals are genetically male (XY chromosomes), usually with female or ambiguous genitalia, although some can have male genitalia with a micropenis.

americantransman. "Beards, Baldness and What's in Your Pants." *American Trans Man*, American Trans Man, 15 Apr. 2012, americantransman.com/2010/04/12/beards-baldness-and-whats-in-your-pants/. Accessed 9 Aug. 2019.

All patients demonstrated growth of the penis during treatment. The mean increase rate (153%) in the first 4 weeks of treatment was higher than that (118%) of the second 4 weeks...In conclusion, transdermal dihydrotestosterone therapy is an effective and relatively safe modality in the treatment of microphallus.

Choi, Seung K., et al. "Transdermal Dihydrotestosterone Therapy and Its Effects on Patients with Microphallus." *Journal of Urology*, vol. 150, no. 2 Part 2, Aug. 1993, pp. 657–660, 10.1016/s0022-5347(17)35576-3. Accessed 9 Aug. 2019.

3) Hair loss: This is admittedly not the biggest concern I have but it is still an effect of DHT blockers that can not be overlooked. My hair is a large part of my identity as a non binary person and although I could deal with hair loss it would cause dysphoria and a loss of self confidence in general that I would like to avoid. There is ample evidence in both cisgender men and transgender men that DHT blockers are effective in preventing male-pattern baldness.

Hair loss may begin soon after beginning hormone therapy, and is dependent on genetic factors...

Management is similar to that in non-transgender men. Over the counter minoxidil, 5-alpha reductase inhibitors, and surgical approaches may be used. The 5-alpha reductase inhibitor finasteride blocks conversion of testosterone to the potent androgen dihydrotestosterone. Finasteride 1mg daily (Propecia) is approved for male pattern baldness.

"Overview of Masculinizing Hormone Therapy | Transgender Care." *Ucsf.Edu*, 2019, transcare.ucsf.edu/guidelines/masculinizing-therapy.