Selective Androgen Receptor Modulator GTx-024: A New Effective Treatment for Cancer Cachexia?

Anorexia-cachexia syndrome (ACS), a negative spiral of diminished appetite and weight loss (lean body mass), is a common problem in many kinds of cancer, where it not only leads to patient weakness and diminished function but is also associated with shorter survival. While it’s possible that the ACS is a late effect that might be an irreversible product of progression of an underlying cancer, it may also be that ACS directly contributes to a patient’s decline by making them unable to tolerate further cancer therapy.

GTx-024, also now known as Ostarine™ or enobosarm, is a selective androgen receptor modulator (SARM), which activates the androgen (male hormone) receptor and leads to the activation of a wide range of genes in the cell, the net result of which being increased muscle mass, increased bone mass, and often an increase in mood, energy level, sense of well being, and libido. Not surprisingly, these are the exact opposite effects we routinely see in men placed on androgen suppression as a common (and effective) treatment for prostate cancer. Risks include increased hair growth/virilization in women, prostate stimulation and hyperplasia (excess growth) in men, elevated red blood cell counts (potentially to levels above normal), decrease in HDL cholesterol (the “good cholesterol” associated with exercise and decreased risk of cardiac events), and potentially abnormalities in liver function tests.

The phase I and II studies in patients with cancer-associated weight loss thus far have pretty consistently shown that treatment with daily oral GTx-024 leads to a modest (typically 1-2 kg) increase in lean body mass after 16 weeks, while recipients of placebo had no change or a trend toward slight further weight loss. The GTx-024 studies also assessed physical function with a stair climb function, assessing both the time required to ascend stairs and “power”. The pattern is the same as with body mass: there is a modest but statistically significant improvement in stair climb function in recipients of GTx-024, but little or no change in recipients of placebo. Here are some figures that represent the results in the subset of patients with NSCLC, for instance:
In addition, improvement in function on the stair climb exercise was also associated with an improvement in quality of life on an “anorexia-cachexia scale” (so the questions were specifically related to eating and weight issues, not more global quality of life). More importantly, one subset analysis of this work also suggested that a worse survival associated with weight loss could be abrogated with the addition of GTx-024.

Because ACS is a particularly common problem in NSCLC, and the early results with GTx-024 looked quite favorable in NSCLC patients, the company developing GTx-024 (GTx) is conducting two trials in which patients with NSCLC who will be randomized to receive GTx-024 or placebo while receiving either a combination of a platinum with a taxane chemotherapy, such as Taxol (paclitaxel) or Taxotere (docetaxel) in the “POWER-1” trial, or a platinum with a non-taxane chemo in the “POWER-2” trial:
The studies will be designed to look at the primary endpoints of lean body mass and physical function after 84 days on treatment.

I must admit that I have had somewhat mixed feelings about the development of a potentially expensive supportive care medication that may or may not have “clinically significant” changes for patients, even if a test that is custom-selected to make a novel therapy look favorable shows a statistically significant benefit. I’m not sure that a therapy that could end up costing patients a few hundred dollars per month in a co-pay would be meaningfully valuable if it leads to a

For now, I’m certainly interested in following these trials and the outcome of GTx-024. The early work offers hope that it may be a valuable supportive medication for lung cancer patients and likely also others with advanced cancers.