Managing Anorexia and Cachexia in Cancer Patients

Cachexia and anorexia are major complications that many cancer patients will face. Anorexia is present in 15% to 25% of all cancer patients at diagnosis. It is estimated that cachexia is the actual cause of death in 20% to 40% of cancer patients. Malnutrition in cancer patients is an indication of unfavorable outcomes, such as increased morbidity and mortality; as well as decreased quality of life. Weight loss that occurs prior to the initiation of chemotherapy is a predictor of shortened survival. Proper nutrition is important in cancer patients to help maintain weight and the body’s nutritional stores. This helps to minimize the nutritional impact on symptoms and will improve quality of life. Early intervention using appropriate nutrition and pharmacologic-symptom management strategies can keep weight loss at bay. Megestrol acetate and dronabinol are the two drugs that have been studied the most in cancer patients with anorexia and cachexia; thalidomide, oxandrolone and cyproheptadine have also been studied, but not as extensively.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Megestrol Acetate and Megace ES*</th>
<th>Dronabinol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of Action</td>
<td>Antagonizes the metabolic effects of catabolic cytokines</td>
<td>Mechanism of appetite stimulation is unknown</td>
</tr>
<tr>
<td>Side Effects</td>
<td>Adrenal suppression, diabetes, thromboembolism</td>
<td>CNS depression, tachycardia, anxiety, paranoia, confusion</td>
</tr>
<tr>
<td>Recommended Dose</td>
<td>800mg per day</td>
<td>Initial dose of 2.5mg, may titrate up to a maximum of 20mg/day</td>
</tr>
</tbody>
</table>
| Availability and Cost         | Megestrol Acetate 40mg/ml (480ml) $286.46  
Megace ES 625mg/5ml (150ml) $612.17 | 2.5mg (60 capsules) $260.00  
5mg (60 capsules) $680.00  
10mg (60 capsules) $960.00 |
| Megestrol vs. Dronabinol      | n=159  
dose: 800mg orally daily plus placebo capsules  
75% reported increased appetite  
14% reported a ≥10% weight gain above baseline; physician obtained | n=152  
dose: 2.5mg orally twice daily plus placebo liquid  
49% reported increased appetite (p=0.0001)  
5% reported a ≥10% weight gain above baseline; physician obtained (p=.0009) |
| Comments                      | Megestrol Acetate has been shown to improve appetite, to induce weight gain and to improve quality of life. Megestrol acetate was shown to be superior to dronabinol in the treatment of anorexia in cancer patients. The combination did not demonstrate additional benefits | There is inconsistent evidence of the clinical effectiveness of dronabinol in cancer patients |

Sipuleucel-T (Provenge) Approved by FDA for Prostate Cancer

**Indication:** Asymptomatic or minimally symptomatic metastatic castration resistant prostate cancer

**How it works:** Sipuleucel-T is “treatment vaccine.” A patient’s antigen presenting cells (APCs) are exposed to prostatic acid phosphatase (PAP), an antigen present in 95% of prostate cancers and GM-CSF. The patient’s APCs are “activated” to target PAP. The cells are infused into the patient where APCs stimulate the immune system to attack PAP antigens on prostate cancer cells.

**Dosing:** The dosing schedule consists of 3 infusions, approximately 2 weeks apart. (Note: each dose requires leukapheresis and coordination with Dendreon.)

- **Step 1:** The patient undergoes leukapheresis and cells are sent to sipuleucel-T’s manufacturer, Dendreon.
- **Step 2:** Dendreon prepares the patient-specific dose of sipuleucel-T for infusion.
- **Step 3:** The blood product is sent to the patient’s physician for infusion.

**Administration:** Premedicate with acetaminophen (650 mg) and diphenhydramine (50 mg).

Infuse of 60 minutes.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Group</th>
<th>TTP (weeks)</th>
<th>OS (months)</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small EJ, J Clin Oncol. 2006; 24(19):3089-94</td>
<td>Sipuleucel-T (n = 82)</td>
<td>11.7</td>
<td>25.9</td>
<td>Rigors &amp; fever were more common in sipuleucel-T group.</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 45)</td>
<td>10.0</td>
<td>21.4</td>
<td>p = 0.052</td>
</tr>
<tr>
<td>Kantoff PW, N Engl J Med. 2010;363:411-22</td>
<td>Sipuleucel-T (n = 341)</td>
<td>14.6</td>
<td>25.8</td>
<td>Chills, fever, headache, myalgia, hypertension, &amp; groin pain were more common in sipuleucel-T group.</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 171)</td>
<td>14.4</td>
<td>21.7</td>
<td>p = 0.63</td>
</tr>
</tbody>
</table>

TTP: time to disease progression; OS: overall survival; *denotes statistically significant

**Commentary:** Sipuleucel-T is a landmark drug, the first cellular immunotherapy, or vaccine, to treat cancer. What is interesting about this drug is that there appears to be no difference it time to disease progression, but there does appear to be 4 month survival advantage. Historically, immune-based therapies have shown the greatest single agent activity when given early is the disease course, not after metastatic spread. This certainly opens up the door to future research endeavors of sipuleucel-T in early stage prostate cancer.

The 3 infusion course costs $93,000 in total. This equates to ~$23,000/month of life gained (Longo DL. N Engl J Med 2010;363:479-81). Dendreon has specialists on call to assist in determining patient coverage and coordinating treatment schedules and drug orders. Visit [www.Provenge.com](http://www.Provenge.com) or call (877) 336-3736 for more information.

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