**Title of Research**
Understanding How Obesity Influences Immunotherapy in Melanoma Patients

**Lead Researcher**
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**Data Sharing Agreement Date**
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**Summary of Research**
More than 30% of adults in the U.S. are obese, and this number is expected to rise over the next decade. Included in the list of health concerns that plague obese and overweight individuals is an increased risk for some cancers. Together, these factors ensure that an increasing percentage of future cancer patients will be obese. Cancer treatment has shifted in recent years toward immunotherapy where the patient's own immune system is engaged to fight cancer. However, the immune system is weakened by chronic inflammation and metabolic abnormalities associated with obesity. Thus, Teague and colleagues predict that obese cancer patients may not derive the same benefits from immunotherapy that other patients do, and may require additional or alternative approaches. In order to move forward, this hypothesis needs to be tested and there is an opportunity to do this by simply looking at existing data already collected from immunotherapy clinical trials.

The clinical trial NCT00094653 reported in 2010 (Hodi et al, NEJM) provides an opportunity to make such a determination in a group of patients receiving anti-CTLA-4 ipilimumab with or without gp100 peptide vaccine. While progression-free survival and overall survival were reported in this publication, no information on body mass index (BMI) was provided. BMI can easily be calculated for each patient by dividing their weight (kg) by height (m) squared. The researchers propose that by plotting BMI versus time of progression-free survival (PFS) or overall survivial (OS), a correlation between BMI and outcomes could be rigorously assessed. This type of retrospective analysis could provide valuable information on patient populations that may require additional interventions or different immunotherapy regimens for the treatment of cancer, or alternatively could eliminate BMI as an influential factor in patient outcomes.

To add to this study rationale, using a pre-clinical mouse model of melanoma, the Teague lab has discovered that obese animals respond poorly to combination immune checkpoint blockade with anti-PD-1 and anti-CTLA-4. This corresponds with impaired T cell function within tumors.

While the researchers are still exploring the molecular and cellular mechanism underlying this immune dysfunction, it is imperative to determine if obesity also influences outcomes in human melanoma patients receiving similar immunotherapies.

**Study Design**
A retrospective analysis will be performed of melanoma patient BMI versus overall survival during immunotherapy with ipilimumab alone or with gp100 peptide vaccine.

The researchers hypothesize that responses to cancer immunotherapy are compromised in obese patients with melanoma. They predict this will be reflected as reduced overall survival in patients with higher BMI. They plan to plot patient BMI on the y-axis versus duration of progression free survival (PFS) or overall survival (OS; time in months) on the x-axis. If this hypothesis is correct, the researchers expect to see an inverse correlation between BMI and PFS or OS.

The primary objective will be to determine whether obesity (high BMI) influences progression-free survival or overall survival in melanoma patients being treated with ipilimumab alone or with gp100 peptide vaccine. The secondary objective will be to determine if BMI influences outcomes differently in male and female patients.

**Study Population**
The ressearchers are requesting data on the sex, height and weight (for BMI calculation), overall survival and progression-free survival for patients with metastatic melanoma reported in Hodi et al, NEJM 2010 Figure 1A. This includes 137 patients treated with ipilimumab, and 403 treated with ipilimumab plus gp100.

**Funding Source of Research**
The researchers do not anticipate any cost associated with this retrospective analysis of existing data. However, the Teague lab is sufficiently supported by a pilot grant from Saint Louis University for research into the impact obesity has on cancer immunotherapy. These funds could be utilized for any unanticipated costs associated with our proposed analysis.

**Requested Study**
CA184-002 (NCT00094653): MDX-010 Antibody, MDX-1379 Melanoma Vaccine, or MDX-010/MDX-1379 Combination Treatment for Patients With Unresectable or Metastatic Melanoma