Title of Research
Association of Obesity with Clinical Outcomes in Metastatic Melanoma Patients Treated with Immunotherapy

Lead Researcher
Jennifer McQuade

Primary Affiliation
University of Texas MD Anderson Cancer Center (MDACC), Melanoma Medical Oncology, Houston, Texas

Data Sharing Agreement Date
February 16, 2017

Summary of Research
Preclinical and clinical research support that obesity can promote cancer initiation, progression, therapeutic resistance, and decreased survival in many types of cancer. Many of these effects are mediated by increased insulin and insulin-like growth factors. There is also evidence that obesity may impact immune function. Currently very little is known about the clinical associations, prognostic significance, or therapeutic impact of obesity in melanoma. An improved understanding of the relationship between metabolic phenotypes and the tolerance and efficacy of contemporary therapies could lead to clinical impact through improved risk stratification and direct interventions (dietary or pharmacological).

In preliminary studies, the clinical factors and outcomes associated with body mass index (BMI) were analysed in a cohort of 599 metastatic melanoma patients with activating BRAF mutations treated with dabrafenib and trametinib in randomized clinical trials. Unexpectedly, this analysis demonstrated that obese patients had significantly improved progression-free survival and overall survival compared to normal weight patients. This difference remained significant on multivariate analysis correcting for multiple prognostic factors (i.e. age, gender, performance status, stage, LDH, and prior immunotherapy). Interestingly, this association was significant in men, but not in women.

The impact of obesity on clinical outcomes in patients treated with immunotherapy is unknown. The increased use of immunotherapy in metastatic melanoma, the predictive significance of PD-L1 expression, and the prognostic significance of immune infiltrates in patients with clinically localized and regional disease further support the rationale to study these associations.

Study Design
The researcher proposes to examine the association of BMI with outcomes in metastatic melanoma patients previously enrolled in BMS-sponsored prospective clinical trials involving checkpoint inhibitors. The primary objective is to analyze the association of BMI with clinical outcomes including objective response rate (ORR), progression-free survival (PFS), and overall survival (OS). Secondary objectives include analyzing the interaction between other clinical characteristics and BMI and clinical outcomes, including gender, age, and concomitant medications; and analyzing the association of BMI with immune-related adverse events, pharmacokinetics, and PDL1 expression.

The hypothesis is that higher BMI is associated with improved outcomes in these patients, with the association between BMI and outcomes remaining significant after controlling for other clinical characteristics associated with obesity, specifically comorbidities and medications used by patients with metabolic syndrome.

Study Population
This study would examine the study population of CA184-024, a multi-center, randomized, double-blind, two-arm, phase III study in patients with untreated stage III (unresectable) or IV melanoma receiving dacarbazine

plus 10 mg/kg ipilimumab (MDX-010) vs. dacarbazine with placebo. This comprises 250 patients who received dacarbazine + ipilimumab, and 252 who received dacarbazine with placebo.

Funding Source of Research
All analyses will be conducted independently at MDACC; no funds are requested from BMS to support this study

Requested Study
NCT00324155