Title of Research
Early Markers of Clinical Outcome to Ipilimumab Therapy for Advanced Melanoma

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Data Sharing Agreement Date
June 6, 2017

Summary of Research
A subset of advanced melanoma patients respond with significantly improved survival to therapy with ipilimumab (Yervoy), an immune checkpoint inhibitor. The ability to predict which patients are unlikely to benefit would help guide decisions on duration and choice of therapy. Small studies suggest that early changes in absolute lymphocyte count (ALC), absolute eosinophil count (AEC), and serum lactate dehydrogenase (LDH) may predict response and survival for individuals receiving ipilimumab. However, the small sample sizes and differences in methods and reporting limit the ability to validate and compare performance of these markers. There is also very preliminary evidence that changes in LDH and ALC may be of value for the PD1 inhibitors, another type of immune checkpoint inhibitor. A small study indicates that changes in AEC may predict the risk of immune-related adverse events. However, a larger and more comprehensive evaluation of the validity and nature of these associations is required before clinical use of such markers can be realistically considered.

Study Design
This will be a retrospective secondary cohort analysis of data from some 1,400 participants treated with ipilimumab therapy for advanced melanoma in existing clinical studies, who were alive at week 6.This landmark time was chosen on the basis that labs were planned at week 6across most studies, and this is a relatively early time point following commencement of therapy that allows sufficient time for changes in the laboratory markers to take effect. The research will evaluate changes in three potential laboratory markers (ALC, AEC, and LDH) at week 6 compared to pre-treatment for association with overall survival, best response and immune-related adverse events.

Study Population
Participants treated with ipilimumab therapy for advanced melanoma

Funding Source of Research
No external funding for project

Requested Study
CA184-002 (NCT00094653): A Randomized, Double-Blind, Multicenter Study Comparing MDX-010 Monotherapy, MDX-010 in Combination with a Melanoma Peptide Vaccine, and Melanoma Vaccine Monotherapy in HLA-A2*0201-Positive Patients with Previously Treated Unresectable Stage III or IV Melanoma

CA184-004 (NCT00261365): An Exploratory Study to Determine Potential Predictive Markers of Response and/or Toxicity in Patients With Unresectable Stage III or IV Malignant Melanoma Randomized and Treated With Ipilimumab (MDX-010/BMS-734016) at Two Dose Levels

CA184-007 (NCT00135408): Randomized, Double-Blind, Placebo-Controlled Phase II Study Comparing the Safety of MDX-010 (BMS-734016) Administered With or Without Prophylactic Oral Budesonide (Entocort EC) in Patients with Previously Treated Unresectable Stage III or IV Malignant Melanoma

CA184-008 (NCT00289627): A Multi-Center Single Arm Phase II Study of MDX-010 (BMS-734016) Monotherapy in Patients with Previously Treated Unresectable Stage III or IV Melanoma

CA184-021 (NCT00077532): Monoclonal Antibody with or without gp100 Peptides plus Montanide ISA-51 in Treating Patients with Stage IV Melanoma

CA184-022 (NCT00289640): A Randomized, Double-Blind, Multi-center, Phase II Fixed Dose Study of Multiple Doses of Ipilimumab (MDX-010) Monotherapy in Patients with Previously Treated Unresectable Stage III or IV Melanoma

CA184-024 (NCT00324155): 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

CA184-042 (NCT00623766): A Multi-Center Phase II Study to Evaluate Tumor Response to Ipilimumab (BMS-734016) Monotherapy in Subjects with Melanoma Brain Metastases