

**Title of Research**

*Impact of Concomitant Statin Use on Efficacy and Toxicity of Ipilimumab*

**Lead Researcher**

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**Data Sharing Agreement Date**

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**Summary of Research**

Recent research suggests that statins – used widely to lower blood cholesterol levels – may have immunosuppressive and anti-inflammatory effects. These findings have far reaching implications for patients receiving immune checkpoint inhibitors such as ipilimumab for cancers who are also taking statins.

For example, in patients with blood cancers who received stem cell transplants, statin use by the donor was shown in a retrospective analysis to reduce the risk of acute graft-versus-host disease (GVHD), while statin use by both donor and recipient eliminated one type of acute GVHD in all four patients studied. Another retrospective analysis of blood cancer patients receiving stem cell transplants found that recipient statin treatment at the time of transplantation significantly decreased the risk of chronic GVHD, but also compromised the beneficial graft-versus-tumor effect. Statins have also been shown to reduce lung inflammation in patients with community-acquired pneumonia and to reduce C-reactive protein serum levels as a marker for inflammation in a case-control study. In animal models, statins have proven effective in the treatment of autoimmune diseases

This study will examine effects of statin use on the efficacy of ipilimumab to ensure that continuation of statins does not impair immune activation and melanoma control. The impact of statin use on the incidence of immune-related toxicities will also be examined, since the anti-inflammatory effects of statins may reduce toxicity.

Data sets will be examined from three phase III trials of ipilimumab to determine the percentage of patients who were also using statins. Previously reported endpoints of efficacy and toxicity will be compared with findings from statin non-users. If differences are identified, their statistical significance will then be examined and could provide a rationale for examining other data sets.

**Study Design**

One or more phase III trials of ipilimumab will be examined to determine the percentage of patients in each treatment arm with and without statin use. Efficacy endpoints such as overall response rate, progression-free survival and landmark survival will be compared between statin users vs. non-users within each treatment group. Similarly, the incidence of severe or life-threatening (grade 3 or 4) toxicities will be compared between statin users and non-users within the same treatment group.

If statins are found to reduce ipilimumab efficacy, future trials could restrict concomitant statin use and thereby improve response. If statins diminish ipilimumab toxicity without affecting efficacy, then they may add an important new drug class for managing immune related adverse events. The impact of statins on ipilimumab would also have important implications for optimizing trials of nivolumab.

**Study Population**

The study population will be patients with stage III or IV melanoma participating in one of the three cited phase III trials of ipilimumab.

**Funding Source of Research**

N/A

**Requested Study**

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