CASE STUDY: MAY 2014

**CTLA4 blockade broadens the peripheral T-cell receptor repertoire**


**BACKGROUND**

- Blockade of the negative immune regulatory checkpoint cytotoxic T-lymphocyte-associated protein 4 (CTLA4) results in long-lasting responses in a minority of individuals with advanced melanoma
- Phase I and II testing of the antitumor activity of tremelimumab (treme) demonstrated durable tumor regressions, most of them lasting beyond 5 years, in approximately 10% to 15% of patients with metastatic melanoma

**AIM**

To evaluate the immunomodulatory effects of CTLA4 blockade with treme in peripheral blood mononuclear cells (PBMCs)

**METHODS**

Peripheral blood samples were collected from 21 subjects with metastatic melanoma and PBMCs were obtained. PBMCs in four healthy donors were used as a control

1. Baseline: PBMCs → gDNA extraction → immunoSEQ™
2. Treme treatment
3. 30–60 days: PBMCs → gDNA extraction → immunoSEQ

**RESULTS**

- Higher TCRB diversity is associated with subjects who had treatment-related toxicities

**CONCLUSIONS**

- Treme increases the diversity of the circulating T-cell repertoire. This represents a pharmacodynamic effect of how this class of antibodies modulates the immune system
- Higher TCRB diversity is associated with subjects who had treatment-related toxicities
- Tumor-infiltrating lymphocyte populations from tumor biopsies in subjects receiving anti-CTLA4 therapy are being evaluated in other studies to determine the possibility of using the immunoSEQ Assay to identify biomarkers of response

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