
Supplemental Data

Supplemental Figure 1. CONSORT Diagram

Supplemental Table 1. Patient Demographics.

Supplemental Table 2. Worst grade adverse event for individual patients that occurred within the first twelve weeks of treatment (induction dose-limiting toxicity period). Adverse events recorded multiple times for any patient are reported only once according to the worst grade.

Supplemental Table 3. Summary of grade 3 and grade 4 events incidence at each dose level for all events and those events possibly, probably, or definitively related.

Supplemental Figure 2. High-power H&E and CD31 stained post treatment biopsy of intratumoral vessels. The endothelial cells appear morphologically columnar. CD31 staining is concentrated at the interendothelial junctions (arrows).

Supplemental Figure 3. Illustrations of the variation in pathologic responses to treatment. Examples of intermediate and no response.

Supplemental Figure 4. Individual response of CCR7⁺CD45RO⁺ and CCD7⁻CD45RO⁺ of CD4⁺ and CD8⁺ T cells in melanoma patients treated with ipilimumab (3mg/kg), ipilimumab (3mg/kg) plus bevacizumab, or ipilimumab (10mg/kg) plus bevacizumab.

Supplemental Table 4. Best overall response in ipilimumab plus bevacizumab treated patients per RECIST criteria by treatment cohort.

Supplemental Figure 5. A. Axial CT section of the chest at baseline demonstrates two nodules in the right lung, the dominant one in the lower lobe (white arrows). B. Follow-up CT 3 months after start of treatment demonstrates resolution of one of the nodules and no change in the other nodule. C. Axial CT section 8 months after start of treatment demonstrates complete resolution of the dominant lung nodule.

Supplemental Figure 6. Response kinetics in treated patients. Baseline tumor measurements are standardized to zero. A. Entire treatment population (cohorts 1-4). B. Cohort 2 patients (MTD). Horizontal line PD = progressive disease representing 20% increase. Horizontal line PR represents 30% decrease from baseline. Filled in circle depicts radiographic development of new sites of disease.

Supplemental Figure 7. Kaplan-Meier estimates for time-to-progression in the entire treated population (A) and by treatment cohort (B). Kaplan-Meier estimates for overall survival in the entire treated population (C) and by treatment cohort (D).

Appendix A. Clinical protocol.