

SUPPLEMENTAL FIGURE S1: Study design: Treatment with Ipilimumab was administered on weeks 1, 4, 7 and 10 at 10 mg/kg during induction. Radiation therapy was administered in 3 fractions (monday-wednesday-friday) at week 4. Then, Ipilimumab was administered intravenously over 90-minutes at 10 mg/kg every 12 weeks starting at week 24, for as long as the treating physician believes that there is a clinical benefit or for as long as patient is tolerant of therapy.

SUPPLEMENTAL FIGURE S2: Analysis of CD4+ and CD8+ T cells in the blood to determine if radiotherapy could determine pharmacodynamics changes: Blood immune monitoring was realized for each patient at baseline (T0), at W4 (before second injection of ipilimumab) and at W6 (after radiotherapy and before third injection of ipilimumab).

SUPPLEMENTAL FIGURE S3: Description of treatments administered in patients who progressed after the “Mel Ipi Rx” study.

SUPPLEMENTAL FIGURE S4: Boxplot of the EXP-TGR for the non-irradiated lesions, according to progressive disease.

SUPPLEMENTAL FIGURE S5: (A) Progression-free survival according to the fold change in CD8 from baseline to week 4. A high fold change in CD8 was significantly correlated to progression-free survival. (B) Overall survival according to the fold change in CD8 from baseline to week 6. A high fold change in CD8 was not significantly correlated to overall survival.

SUPPLEMENTAL FIGURE S6: Evolution of innate immune cells. A. Absolute lymphocytes, monocytes and neutrophils in patients with CR, PR and SD (n=12) and in patients with PD (n=4) at baseline, W4 (after ipilimumab treatment W4) and W6 (after radiotherapy + ipilimumab treatment W6). B. NLR (Absolute neutrophils count (ANC) / Absolute lymphocyte count) or dNLR (ANC/ (WBC-ANC)) in patients with CR, PR and SD (n=12) and in patients with PD (n=4) at baseline, W4 (after ipilimumab treatment W4) and W6 (after radiotherapy + ipilimumab treatment W6). Means with 95% CI are shown. P values are indicated on the graphs otherwise not significant.