Auto-immune side effects and efficacy of checkpoint inhibitor in agnostic of cancer site population: from toxicity to improving survival.

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Background: The approval of anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and anti-programmed cell death protein 1 (PD-1) antibodies resulted in significant improvements in disease outcomes for various cancers. PD-1 and CTLA-4 limit immune activation in physiological conditions and prevent autoimmunity, therefore inhibition of these receptors is associated with a wide range of autoimmune side effects. Interestingly, certain treatment-related auto-immune reactions have been shown to correlate with better prognosis suggesting a correlation between auto-immunity and anti-tumor immune responses. We conducted a retrospective analysis to explore this relation in an agnostic of cancer site population treated with checkpoint inhibitors.
Patients and methods: We conducted a retrospective analysis of patients with metastatic melanoma (MM), non-small cell lung cancer (NSCLC) and renal cell carcinoma (RCC) treated from September 2014 to February 2018 at our Institution (Fondazione Policlinico Universitario "A. Gemelli" - IRCCS) and exposed for the first time (in first or subsequent lines) to monotherapy with checkpoint inhibitor (Ipilimumab or Nivolumab or Pembrolizumab). The aim was to correlate the auto-immune adverse events (AE) with progression free survival (PFS). A multivariate analysis was performed with prognostic factor which could limit this unconventional analysis (line of therapy: 1 vs >1, gender: male vs female, cancer site: melanoma vs non melanoma, immune therapy: anti-PD-1 vs anti-CTLA-4).
Results: 140 patients were enrolled: 71 patients (51%) with NSCLC, 57 patients with MM (40%) and 12 patients with RCC (9%). 39 patients developed auto-immune AEs (28%). The PFS in the population with auto-immune AE was 13.5 *vs* 7.5 months (HR: 0.41; 95%CI: 0.25-0.67, p 0.001). Multivariate analysis confirmed that only auto-immune AEs statistically impact on PFS.
Conclusions: Despite the limitation of the retrospective nature of this study and the possible bias due to the peculiar selection of patient, our data showed an interesting association between auto-immune AE and outcomes of checkpoint inhibitor therapy in an agnostic of cancer site population.