

403TIP

CREAM study: Clinical correlation between ipilimumab-Related colitis And intestinal Microbiote in metastatic melanoma patients

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Background: The composition of intestinal flora is able to influence the development of inflammatory gastrointestinal diseases, and the association of inflammatory diseases with specific intestinal microbes is still unknown, because the inflammation itself and its treatment can change the composition of the microbiota. Some bacterial species are essential to maintain mucosal physiological tolerance, although species such as *Bacteroides*, *Clostridium* and *Faecalibacterium* can induce the up-regulation of T-cells and stimulate the production of anti-inflammatory cytokines. Ipilimumab, Nivolumab and Pembrolizumab, a monoclonal anti-CTLA-4 antibody and inhibitors of the PD-1 receptor, respectively, are particularly involved in the up-regulation of lymphocyte system: among their side effects, the most relevant are those immune-mediated such as hypophysitis, thyroiditis and colitis. Within 16 weeks from the start of treatment, about one third of patients develop intestinal inflammation as a result of dysregulation of the immune system of the intestinal mucosa. Therefore, the high incidence of colitis in patients treated with immunotherapy offers the possibility to characterize the intestinal microbiota before the development of immune-mediated inflammation.

Trial design: Our study is a single-center observational study of clinical and biological parameters prospectively stratified. Specifically, we collect from patients eligible for immunotherapy a blood sample to analyze serum cytokines levels and, at the same time, a sample of fecal material at baseline and every 6 weeks of treatment: we plan to enroll 40 patients in 6 months. According to preliminary data already published in the literature, we expect to find an alteration of the intestinal microbiota in patients with metastatic melanoma treated with immunotherapy. Once we'll identify the presence of an alteration of the microbiota, we want to assess whether there is any correlation with the patient's clinical outcome.

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