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Early onset of endocrine alterations during PD-1 blockade in advanced NSCLC patients

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Background: Immune checkpoint inhibitors have been widely studied in recent years for solid tumors treatment, including lung cancer. Despite advantages observed in term of survival, new toxicities, such as endocrinopathies, have been observed. The most common are thyroid dysfunctions, hypophysitis and adrenal insufficiency. Diabetes mellitus and low level of testosterone are observed with anti-CTLA4 antibodies, but no data for anti-PD-1 and anti-PD-L1 are reported so far.

Methods: Patients with histological diagnosis of squamous NSCLC, eligible for treatment with nivolumab, with ECOG PS 0-2 and adequate organs function were enrolled in our observational prospective study. All patients underwent blood sampling before starting treatment, after one and two months. All samples were analyzed for adenopituitary hormones (LH, FSH, ACTH, PRL, TSH) and for hormones secreted by target glands (FT3, FT4, 17- β -estradiol, testosterone, cortisol).

Results: We enrolled 11 patients (6 M, 5 F; median age 65 y, range 44-82 y) affected by squamous NSCLC, receiving nivolumab in second line treatment. Three patients had hypothyroidism treated with levothyroxine in past medical history. The majority of patients (72.7%) showed endocrine alterations during treatment, three of which were symptomatic. Three males showed a reduction of testosterone level, in one case associated with decreased libido. A woman had a raised testosterone with hirsutism. Two patients experienced an increase in LH and FSH level and one patient a reduction. Moreover, we observed two cases of hyperthyroidism, one of which symptomatic in a patient with hypothyroidism in past medical history, two cases of increased ACTH level, one case of PRL reduction, one of 17-B-estradiol raise, one of cortisol reduction and one of cortisol raise. In all the cases endocrine alterations onset early during the treatment.

Conclusions: We observe high rate of endocrine alterations in patients receiving nivolumab, in most cases asymptomatic. Many alterations observed are not usually evaluated and symptoms are often underestimated. More and wider studies could help to manage symptoms for a better quality of life and to investigate the mechanisms underlying endocrine disorders.

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