News Release

Title

Patients with anti-thyroid antibodies are prone to develop destructive thyroiditis by nivolumab: a prospective study

Key Points

- **Cancer immunotherapies have been widely used and improved prognosis in patients with advanced malignancies.**
- **In contrast, cancer immunotherapies cause several adverse events.**
- **To clarify the incidence of endocrine irAEs induced by nivolumab, all patients treated with nivolumab at Nagoya University Hospital were prospectively evaluated with regard to endocrine adverse envets.**
- **The prevalence of positive anti-thyroid antibodies at baseline was significantly higher in the group developing destructive thyroiditis (50%) compared to that not developing thyroiditis (1.7%).**
- **Nivolumab treatment can be restarted under the appropriate management for the impaired endocrine functions.**
- **This study indicate that evaluating the antibodies before treatment may help identify patients with a high risk of thyroidal irAEs and may have significant clinical benefit.**

Summary

Immune checkpoint inhibitors activate T cells and show anti-tumor effects though the increased immune responses against cancer cells. Nivolumab, an immune checkpoint inhibitor, has been shown as an effective treatment for unresectable metastatic melanoma, non-small cell lung cancer, renal cell carcinoma, head and neck cancer, Hodgkin lymphoma and gastric cancer. However, these medicines can cause immune-related adverse events (irAEs). To examine the incidence of endocrine irAEs induced by nivolumab, 66 patients treated with nivolumab at Nagoya University Hospital were prospectively evaluated with regard to pituitary hormones, thyroid function, anti-thyroid antibodies, and glucose levels every 6 weeks after the initiation of nivolumab for a period of 24 weeks. Four out of 66 patients developed destructive thyroiditis. The prevalence of positive anti-thyroid antibodies (anti-thyroglobulin antibodies and/or anti-thyroid peroxidase antibodies) at baseline was significantly higher in the group developing destructive thyroiditis compared to that not developing thyroiditis. During the 24 weeks post-initiation of nivolumab therapy, the cumulative incidence was significantly higher in the patients with positive anti-thyroid antibodies compared to those without them. Our real-world data showed that destructive thyroiditis was an endocrine irAE that was frequently induced by nivolumab, and was significantly associated with positive TgAb and/or TPOAb before treatment. Our findings indicate that evaluating these antibodies before treatment may help identify patients with a high risk of thyroidal irAEs and may have significant clinical benefit.

Research Background

Immune checkpoint inhibitors, including anti-programmed cell death-1 (PD-1) antibodies, have become promising treatments for a variety of advanced malignancies. However, these medicines can cause immune-related adverse events (irAEs), including endocrinopathies.

To clarify the incidence of endocrine irAEs induced by nivolumab, all patients treated with nivolumab at Nagoya University Hospital were prospectively evaluated with regard to pituitary hormones, thyroid function, anti-thyroid antibodies, and glucose levels every six weeks after the initiation of nivolumab for a period of 24 weeks since November 2nd 2015.

Research Results

Sixty-six patients treated with nivolumab were enrolled in this study. Four out of 66 patients developed destructive thyroiditis. The prevalence of positive anti-thyroglobulin antibodies (TgAb) and/or anti-thyroid peroxidase antibodies (TPOAb) at baseline was significantly higher in the group developing destructive thyroiditis (3 of 4) compared to that not developing thyroiditis (3 of 62) ($p = 0.002$). There were no significant differences in other clinical variables between the groups. There were no endocrine irAEs other than destructive thyroiditis during the 24 weeks. The prevalence of TgAb and/or TPOAb at baseline was not associated with the development of other irAEs including pneumonitis, colitis, or skin reactions.

Research Summary and Future Perspective

This real-world data showed that destructive thyroiditis was an endocrine irAE that was frequently induced by nivolumab, and was significantly associated with positive TgAb and/or TPOAb before treatment. These findings indicate that evaluating these antibodies before treatment may help identify patients with a high risk of thyroidal irAEs and may have significant clinical benefit.

Publication

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