

News Release

Title

Pituitary dysfunction induced by immune checkpoint inhibitors is associated with better overall survival in both malignant melanoma and non-small cell lung carcinoma: a prospective study

Key Points

- Immune checkpoint inhibitors (ICIs) have been widely used and improved prognosis in patients with advanced malignancies.
- In contrast, ICIs cause several immune-related adverse events (irAEs).
- To clarify the incidence and clinical characteristics of endocrine irAEs induced by ICIs, all patients treated with ICIs at Nagoya University Hospital were prospectively evaluated with regard to endocrine adverse events. We also analyzed prognosis in the malignant melanoma (MM) and non-small cell lung cancer (NSCLC) patients.
- Pituitary-irAE was observed in 16 patients [four (3.7%) with NSCLC, 12 (18.2%) with MM], which was higher than previously reported.
- In our study cohort, the development of pituitary-irAE predicted better prognosis for both NSCLC and MM when patients were treated with physiological doses of hydrocortisone.

Summary

Immune checkpoint inhibitors (ICIs) activate T cells and show anti-tumor effects through the increased immune responses against cancer cells. ICIs have been shown as an effective treatment for unresectable metastatic melanoma (MM), non-small cell lung cancer (NSCLC), renal cell carcinoma, head and neck cancer, Hodgkin lymphoma, gastric cancer, urothelial cancer, breast cancer and so on. Several immune-related adverse events (irAEs) are reported to be associated with therapeutic efficacy of ICIs, yet whether pituitary dysfunction, a life-threatening irAE, affects overall survival (OS) in patients with malignancies is unclear. This prospective study examined the association of pituitary dysfunction induced by ICIs (pituitary-irAE) with OS of patients with NSCLC or MM. A total of 174 patients (NSCLC, 108; MM, 66) treated with ICIs at Nagoya University Hospital were evaluated for the development of pituitary-irAE. Pituitary-irAE was observed in 16 patients [four (3.7%) with NSCLC, 12 (18.2%) with MM]. All 16 patients had adrenocorticotrophic hormone (ACTH) deficiency and were treated with physiological doses of hydrocortisone. The development of pituitary-irAE was associated with better OS in patients with NSCLC [not reached vs. 441 (95% confidence interval, CI not calculated) days, $P < 0.05$] and MM [885 (95% CI 434 - 1336) vs. 298 (95% CI 84 - 512) days, $P < 0.05$]. In our study cohort, the incidence of pituitary-irAE was higher than previously reported and the development of pituitary-irAE predicted better prognosis for both NSCLC and MM when patients were treated with physiological doses of hydrocortisone.

Research Background

Immune checkpoint inhibitors (ICIs) have recently emerged as promising treatments for advanced malignancies. However, ICIs can cause adverse events, termed immune-related adverse events (irAEs), including pneumonitis, skin toxicities, colitis, and endocrine dysfunction. Endocrine irAEs comprise pituitary dysfunction, adrenal insufficiency, thyroid dysfunction, hypoparathyroidism and type 1 diabetes mellitus (T1DM). Pituitary-irAE is almost always accompanied by adrenocorticotrophic hormone (ACTH) deficiency, a life-threatening disorder, and a retrospective study reported that pituitary dysfunction induced by ipilimumab was associated with better OS in MM patients. However, symptoms of ACTH deficiency, such as fatigue, appetite loss and weight loss, frequently occur in patients with malignancies even if they do not develop pituitary-irAE. As such, pituitary-irAE could have been overlooked unless pituitary hormones were measured regularly, and its incidence may not have been accurately reflected in previous studies. To clarify the association of pituitary-irAE with OS in patients with NSCLC or MM, we performed a prospective study in which endocrine irAEs induced by ICIs were set as a primary endpoint.

Research Results

A total of 174 patients (NSCLC, 108; MM, 66) treated with ICIs at Nagoya University Hospital were evaluated for the development of pituitary-irAE. Pituitary-irAE was observed in 16 patients [four (3.7%) with NSCLC, 12 (18.2%) with MM]. All 16 patients had adrenocorticotrophic hormone (ACTH) deficiency and were treated with physiological doses of hydrocortisone. The development of pituitary-irAE was associated with better OS in patients with NSCLC [not reached vs. 441 (95% CI not calculated) days, $P < 0.05$] and MM [885 (95% CI 434 - 1336) vs. 298 (95% CI 84 - 512) days, $P < 0.05$].

Research Summary and Future Perspective

Our prospective study clarified the exact incidence of pituitary-irAE in a real-world clinical practice and the association of pituitary-irAE accompanied by ACTH deficiency with a better outcome of ICI treatments in both NSCLC and MM when patients were treated with physiological doses of hydrocortisone. Our findings indicate that we should measure pituitary hormones when pituitary-irAE is suspected based on hyponatremia, so that ACTH deficiency in patients treated with ICI will not be overlooked.

Publication

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