

High-dose glucocorticoid treatment vs. replacement in immune checkpoint inhibitor associated hypophysitis (CORTICI): an open, randomised pilot study

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Background: Immune checkpoint inhibitors (ICI) are used to treat an increasing number of oncological entities. Potential immune-related adverse events include hypophysitis, affecting up to 17% of ICI-treated patients. ACTH deficiency is most common and recovery extremely rare, although it has been reported after high-dose glucocorticoids. While current observational data clearly points towards glucocorticoid replacement rather than high-dose glucocorticoid treatment, no randomised study has been performed so far to address this issue.

Methods: The aim of this single-centre, open, randomised (1:) study was to compare high-dose glucocorticoid treatment (1mg/kg of prednisolone for two weeks, followed by tapering until week 7 and a switch to hydrocortisone in week 8) with glucocorticoid replacement therapy (hydrocortisone) over 8 weeks in ICI-associated hypophysitis. The primary outcome was the frequency of hormonal axes recovery, hypothesising that there are no significant differences between groups.

Results: Between May 2019 and September 2022, 20 patients were screened, two failed screening and 18 were randomised to either high-dose glucocorticoid treatment (8 patients) or replacement (10 patients). The 18 patients (61 % women) had a mean age of 66 ± 10 years. The most common oncological diagnosis was malignant melanoma (11 patients, 61 %). Seven patients (38.9 %) were on Nivolumab alone, five (27.8 %) on a combination of Ipilimumab and Nivolumab, five (27.8 %) on Pembrolizumab and one on Atezolizumab (5.6 %). All patients had ACTH deficiency upon presentation. All patients in both the high-dose as well as the replacement group remained ACTH deficient after eight weeks requiring continued need for glucocorticoid replacement.

Conclusions: The frequency of resolution of hypopituitarism is not superior in patients on high-dose compared to replacement therapy. We therefore do not recommend the use of high-dose glucocorticoids for the treatment of ICI-associated hypophysitis, with the exception of optic chiasm compression or other severe compressive symptoms.