Impact of Relacorilant, a Selective Glucocorticoid Receptor Antagonist, on the Immunosuppressive Effects of Endogenous Cortisol

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BACKGROUND
Cortisol is a potent immunosuppressive hormone, which is regulated by the hypothalamic-pituitary-adrenal (HPA) axis. Immunosuppressive effects of corticosteroids can be clinically desirable in cancer patients; however, they also contribute to the development of secondary malignancies and immune-related adverse events (IRAEs). Relacorilant (AG-341), a selective glucocorticoid receptor (GR) antagonist, preserves normal cortisol effects on glucose homeostasis and is currently being evaluated in patients with uncontrolled diabetes mellitus (UMDM) and adrenal insufficiency (AI).

RESULTS
To understand the molecular consequences of GC activity on T-cell activation, Relacorilant alone decreased circulating IL-10, an anti-inflammatory cytokine, in mice. Similarly, patients with adrenocortical cancer (ACC) and excess GC activity showed decreased circulating IL-10 compared to those with normal GC activity (Figures 1A and 1B). These findings support the hypothesis that relacorilant can reverse immune suppression caused by elevated GC activity.

CONCLUSIONS
Relacorilant may reverse the immunosuppressive effects of elevated GC activity, which is clinically important given the prevalence of GC excess in cancer patients. Further studies are needed to evaluate the clinical impact of relacorilant in patients with GC excess and impaired immune function.

REFERENCES


ABSTRACT
Relacorilant is a selective glucocorticoid receptor (GR) antagonist that preserves normal cortisol effects on glucose homeostasis and is currently being evaluated in patients with uncontrolled diabetes mellitus (UMDM) and adrenal insufficiency (AI). Relacorilant may reverse the immunosuppressive effects of elevated GC activity, which is clinically important given the prevalence of GC excess in cancer patients. Further studies are needed to evaluate the clinical impact of relacorilant in patients with GC excess and impaired immune function.