**LCI699 is a Potent Inhibitor of Cortisol Production in Vitro**

**Sara G. Creemers**, L.A. Feelders, F.H. de Jong, G.J.H. Franssen, Y.B. de Rijke, P.M. van Koetsveld, L.J. Hofland

**1** Department of Internal Medicine, division of Endocrinology; **2** Department of Surgery; **3** Department of Clinical Chemistry, Erasmus Medical Center, Rotterdam, the Netherlands

**Poster presented at: ECE 2016**

**DOI**: 10.3252/pso.eu.18ECE.2016

---

**Aim**

To compare the in vitro effects of LCI699, metyrapone, and ketoconazole on cortisol production and steroid hormone profile in human adrenal cells.

**Introduction**

- Ketoconazole and metyrapone are frequently used steriodogenesis inhibitors for treatment of Cushing’s syndrome (CS).
- LCI699 (Osilodrostat) is a new steriodogenesis inhibitor which is known to block 11β-hydroxylase.
- This compound was originally developed for its inhibitory effects on aldosterone production, but appeared to decrease cortisol response to ACTH-stimulation in patients with hypertension.
- LCI699 is now investigated as a potential drug for treatment of CS, but effects on other steriodogenesis enzymes are unknown.

---

**Conclusions**

- LCI699 is a potent inhibitor of basal- and ACTH-stimulated cortisol production in adrenocortical tumor cells.
- LCI699 has only modest inhibitory effects on adrenal androgen production.
- In these conditions, LCI699 seems to block 11β-hydroxylase (CYP11B1), and to a lesser extent 17α,20-lyase activity.
- The absence of strong accumulation of steroid precursors might indicate an inhibition proximal of 3β-HSD.

---

**Results**

1. Effects of LCI699, metyrapone, and ketoconazole on cortisol production in HAC-15 cells

2. Effects of LCI699, metyrapone, and ketoconazole on cortisol production in primary adrenocortical adenoma cultures

3. Effects of LCI699, metyrapone, and ketoconazole on the steroid profile in HAC-15 cells

---

**Methods**

**Cell culture**

- Adrenocortical tumor cell line: HAC-15
- Primary adrenocortical adenoma (ACA) cultures

**Treatment**

- 3 days basal and ACTH (10 nM) stimulated
- LCI699, metyrapone, and ketoconazole (0.01 - 5 μM)

**Measurements**

- DNA: Hoechst dye, representation of cell amount
- Cortisol: chemiluminescence immunoassay system (Immulite 2000XPXi)
- Steroid profile (control and 5 μM treated cells): liquid chromatography/mass spectrometry (LC-MS/MS)