Osilodrostat in patients with persistent or recurrent Cushing's Disease: a real-life single center experience

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Introduction

Medical therapy is a valuable option for patients with peristent or recurrent Cushing's Disease (CD) after transphenoidal adenomectomy (TSA)

Herein we report our real-life experience with the use of osilodrostat, a recently approved *CYP11B1* inhibitor, in patients with CD, who were already on another medical therapy.

Material and Methods

Five patients with persistent/recurrent CD after TSA were switched to osilodrostat due to:

- inadequate control of CD
- significant metyrapone-induced hyperandrogenism and/or
- patient's preference for fewer tablets per day

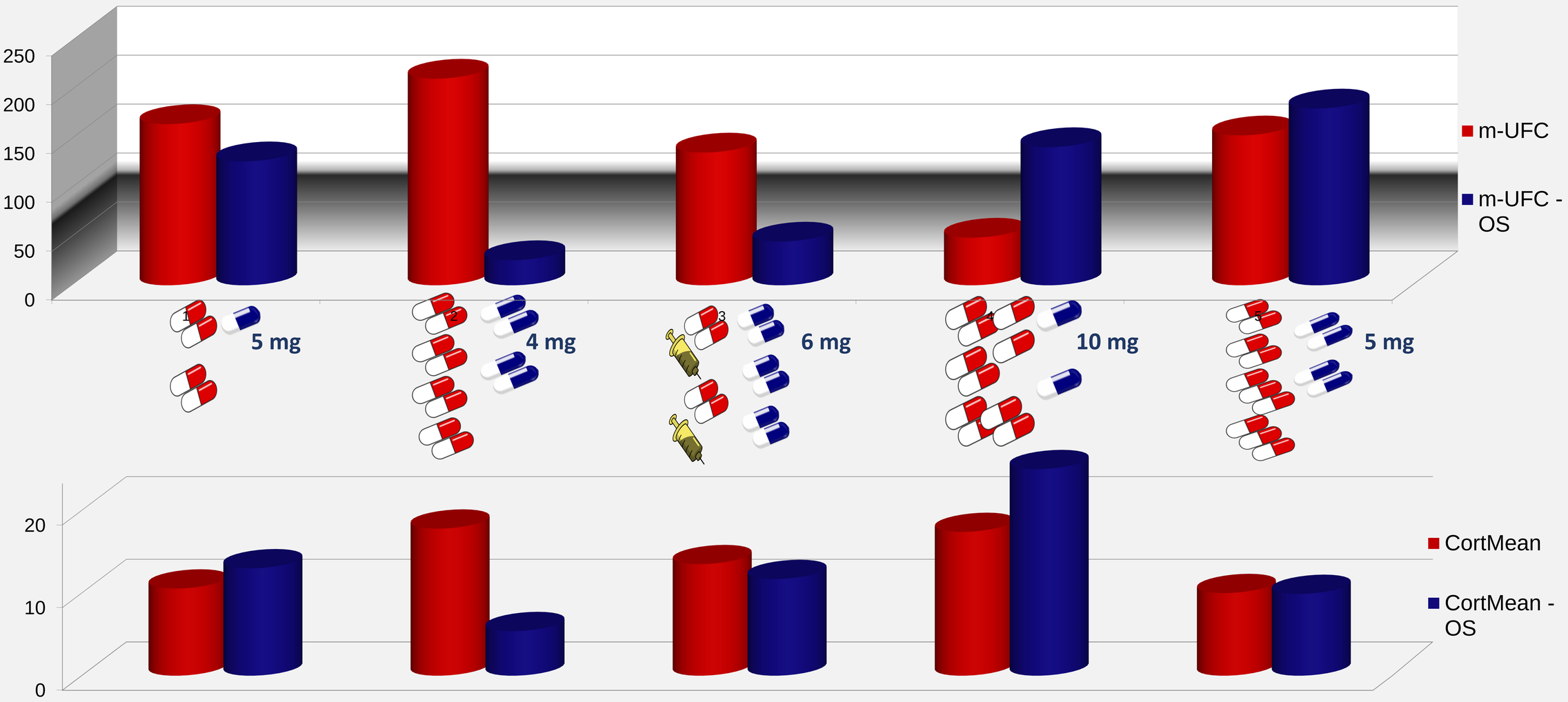
Cushing's control was evaluated by:

- the mean value of two 24h-Urinary Free Cortisol (***mUFC***) levels and
- a 5-point day rhythm of serum cortisol (***CortMean***)

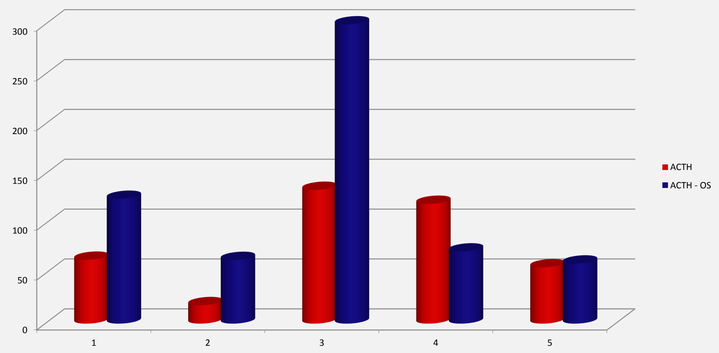
	Patients (n=5)
Gender (Female)	**5**
Age (years)	**52 (33 – 76)**
Previous medication	
a. Metyrapone	**3**
b. Metyrapone + Pasireotide	**1**
c. Metyrapone + Ketoconazole	**1**
Dose of Osilodrostat (mg)	**4 – 10**

Median treatment duration was 45 weeks (range 12-75).

Results



ACTH levels increased in most patients



Comorbidities (diabetes, hypertension, dyslipidemia) ameliorated in patients with improved control

Adverse effects- androgen levels

Patient	Weeks of treatment	Testo (ng/dl)	Testo-OS (ng/dl)	Δ4 (ng/ml)	Δ4-OS (ng/ml)	DHEA-S (μg/dl)	DHEAS-OS (μg/dl)
1	53	**53**	48	**3.7**	2.5	60.2	47.2
2	48	**164**	29	**10.2**	**3.1**	332	79.5
3	75	10	9	1.2	0.9	15	15
4	12	44	**65**	**4.6**	**5.1**	53.8	60.3
5	36	**215**	41	**11.8**	**3.8**	232	161

- One patient developed adrenal insufficiency on 8mg
- Testosterone levels were normalized in patients with high testosterone levels during metyrapone administration

Conclusions

Osilodrostat treatment resulted in better control of hypercortisolemia in patients on other medical treatment but with a better dosing regimen and fewer side-effects.

Based on our preliminary experience, it seems that osilodrostat is a promising effective and safe choice for the treatment of patients with persistent or recurrent Cushing' s disease.

Conflicts of Interest

No conflict of interest