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CHAMPAIN Study: Initial Results From A Phase II Study Of Efficacy, Safety And Tolerability Of Modified-release Hydrocortisones: Chronocort® (Efmody®) Versus Plenadren®, In Primary Adrenal Insufficiency

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Background: Current glucocorticoid replacement regimens for patients with primary adrenal insufficiency (PAI) mean patients wake with either low or undetectable cortisol levels[1], associated with fatigue and a reduced quality of life (QoL)[2]. Plenadren® (Takeda, UK) is a once-daily modified-release formulation of hydrocortisone that replaces daytime cortisol levels whereas Chronocort® (modified-release hydrocortisone hard capsules, Diurnal, UK) when taken twice-daily, has been shown to replicate the normal overnight rise in serum cortisol concentration and provide physiological levels throughout the day. We have undertaken a double-blind, double-dummy, two-way cross-over, randomised, phase II study of efficacy, safety and tolerability of modified-release hydrocortisones: Chronocort® Versus Plenadren®. **Aim:** To test the hypothesis that Chronocort® provides more physiological waking cortisol levels than Plenadren®. **Methodology:** The study was conducted across 8 sites in the UK and Germany. Male and female patients, aged ≥18 with confirmed PAI (defined as morning pre-dose cortisol <50 nMol/l) on stable therapy over the preceding three months and not currently treated with Chronocort®/Plenadren®. Participants with congenital adrenal hyperplasia (CAH), secondary or tertiary AI were excluded. Each participant was randomised on a 1:1 basis to either; treatment sequence I (Chronocort® first) or treatment sequence II (Plenadren® first) taking a 25mg total daily dose for 4 weeks; either Plenadren® 25mg in the morning or Chronocort® 10mg in the morning and 15mg at night with the associated dummy preparation followed immediately by the other treatment. The pre-dose morning serum cortisol level was assayed at baseline and after each treatment period. A physiological morning cortisol level was defined as a pre-dose level of >140nMol/L. Secondary measures included: morning fatigue measured using the Multidimensional Assessment of Fatigue (MAF) questionnaire and the PROMIS® 7b questionnaire; QoL was assessed using the EuroQol 5-level Standardised Health Questionnaire (EQ-5D-5L™); Health-related Quality of Life in Addison's disease (AddiQoL) questionnaire and the 36-Item Short Form Health Survey (SF-36®) questionnaire. **Results:** Of 49 evaluable participants with PAI, 45 achieved a physiological morning cortisol after four weeks of Chronocort® compared with 2 after four weeks of Plenadren® (P<0.0001). The mean (standard deviation) waking cortisol was 422.85 (203.50) vs 36.98 (113.87), respectively. **Conclusion:** Chronocort® provides more physiological waking cortisol levels than Plenadren®. Further analysis will test the hypothesis that waking with physiological cortisol levels improves fatigue and QoL in patients with PAI. 1.Mah PM, et al. Clin Endocrinol (Oxf). 2004;61(3):367-75.2.Wichers M, et al. Clin Endocrinol (Oxf). 1999;50(6):759-65.

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