
Proceedings Paper:
Ross, R.J.M., Merke, D.P., Mallappa, A. et al. (14 more authors) (2024) 7061 Incidence of adrenal crisis in Congenital Adrenal Hyperplasia (CAH) patients during a prospective monitored long-term study of modified-release hydrocortisone (MRHC) capsules, (Efmody). In: Journal of the Endocrine Society. ENDO 2024 Abstracts Annual Meeting of the Endocrine Society, 01-04 Jun 2024, Boston, USA. The Endocrine Society

https://doi.org/10.1210/jendso/bvae163.220

Abstract citation ID: bvae163.220

Adrenal (Excluding Mineralocorticoids)

7061

Incidence of Adrenal Crisis In Congenital Adrenal Hyperplasia (CAH) Patients During A Prospective Monitored Long-Term Study Of Modified-Release Hydrocortisone (MRHC) Capsules, (Efmody)

Richard John M Ross, MBBS FRCP MD[1], Deborah P. Merke, MS MD[2], Ashwini Mallappa, MD MHSc[3], Wiebke Arlt, MD DSc FRCP FMedSci[4], Aude Brac de la Perriere, MD[5], Angelica Linden Hirschberg, MD PhD[6], John D. C. Newell-Price, MD PhD FRCP[1], Alessandro Prete, MD PhD[7], Aled Rees, MD PhD[8], Nicole Reisch, MD[9], Marcus Quinkler, MD[10], Philippe A. Touraine, MD PhD[11], Kerry Maltby, BSc Hons[12], Jo Quirke, BSc (Hons)[13], Naila Aslam, BSc MBBS MRCPCH[14], Helen Coope, PhD[15], and John Porter, MD[16]

[1]University of Sheffield, Sheffield, United Kingdom; [2]NIH, Bethesda, MD, USA; [3]AstraZeneca, Rockville, MD, USA; [4]MRC Laboratory of Medical Sciences (LMS), Birmingham, United Kingdom; [5]HOPITAL NEURO-Cardiologique, Bron Cedex, France; [6]Karolinska Institutet, Stockholm, Sweden; [7]Institute of Metabolism and Systems Research, BIRMINGHAM, United Kingdom; [8]Cardiff University, Cardiff, United Kingdom; [9]Med. Klinik IV, Munich, Germany; [10]Endocrinology in Charlottenburg, Berlin, Germany; [11]GH Pitie Salpetriere, Paris Cedex 13, France;

[12]Diurnal Ltd, Cardiff, United Kingdom; [13]Diurnal, Cardiff, United Kingdom; [14]Diurnal Ltd, a Neurocrine Biosciences company, Cardiff, United Kingdom; [15]NEUROCRINE BIOSCIENCES, rugeley, United Kingdom; [16]Diurnal Ltd., Cardiff, United Kingdom

Disclosure: R.J. Ross: Consulting Fee; Self; Diurnal. **D.P. Merke:** Research Investigator; Self; Diurnal. **A. Mallappa:** Research Investigator; Self; Diurnal. **W. Arlt:** Research Investigator; Self; Diurnal. **A. Brac de la Perriere:** Research Investigator; Self; Diurnal. **A.L. Hirschberg:** Research Investigator; Self; Diurnal. **J.D. Newell-Price:** Research Investigator; Self; Diurnal. **A. Prete:** Research Investigator; Self; Diurnal. **A. Rees:** Research Investigator; Self; Diurnal. **N. Reisch:** Research Investigator; Self; Diurnal. **M. Quinkler:** Research Investigator; Self; Diurnal. **P.A. Touraine:** Research Investigator; Self; Diurnal. **K. Maltby:** Employee; Self; Diurnal. **J. Quirke:** Employee; Self; Diurnal. **N. Aslam:** Employee; Self; Diurnal. **H. Coope:** Employee; Self; Diurnal. **J. Porter:** Employee; Self; Diurnal.

Background: Adrenal crisis is the leading cause of excess mortality in patients with CAH[1]. Retrospective studies report an adrenal crisis incidence of 5-10/100 patient years (PY), with mortality 0.5/100 PY[2]. Modified-release hydrocortisone (MRHC) capsules, (Efmody), replicate cortisol diurnal rhythm and improve androgen control in CAH compared to standard glucocorticoid therapy[2]. Here, we report the incidence of adrenal crisis in CAH patients from a prospective study of MRHC in CAH patients. **Methods:** Patients completing MRHC Ph2 and Ph3 studies were eligible to enter a single-arm, open-label extension study. Study visits occurred at baseline, weeks 4, 12, 24 and 6-monthly thereafter. The primary endpoint was the safety of MRHC over time. Adrenal crisis was defined according to Allolio 2015[3]. MRHC doses were adjusted on the basis of an adrenal insufficiency checklist, and measurement of androstenedione (A4) and 17-hydroxyprogesterone (17-OHP) at 9am and 1pm. **Results:** 91 patients entered the study, mean age 37 years, 68% female, 32% male. 22 discontinued; 11 at patient request, 5 due to pregnancy, 2 undergoing fertility treatment, 2 at physician/sponsor request, 1 due to an AE (carpal tunnel syndrome), and 1 due to death (myocardial infarction). Median treatment duration was 1500 days, range 0.2 to 5.8 years. Median MRHC dose at study entry was 30mg/day, reducing to 20mg/day from 24-weeks until end of study. Signs and symptoms of adrenal insufficiency due to under-treatment were reported for 41 (45.1%) participants, most frequently fatigue which was reported at some point by 41.8% of all participants. Signs and symptoms of overtreatment were reported for 25 (27.5%) participants, most frequently sudden weight gain which was reported at some point by 16.5% of all participants. Signs and symptoms of both over- and undertreatment occurred predominantly during the first 24 weeks. The study encompassed 357 participant years, and 18 adverse events considered indicative of adrenal crisis occurred in 7 participants, giving an incidence rate of 5.043 adrenal crises / 100 PY. **Conclusions:** Data from this longest prospectively monitored study in CAH suggest that the incidence of adrenal crisis on MRHC is at the low end of that reported in retrospective studies and the safety profile of MRHC is otherwise similar to immediate release hydrocortisone.

References: 1. Falhammar H. JCEM 2014 **99** e2715-E212. Merke DP. JCEM 2021 **106** e2063-e20773. Allolio B. EJE 2015 **172** r115-24

Presentation: 6/1/2024