Response to 'Hydrocortisone suspension formulations are not necessarily the same in the treatment of children with congenital adrenal hyperplasia'

Robin Michelet¹, **Johanna Melin^{1,2}**, **Zinnia P Parra-Guillen^{1,3}**, **Uta Neumann⁴**, **Martin J Whitaker⁵**, **Viktoria Stachanow^{1,2}**, **Wilhelm Huisinga⁶**, **John Porter⁵**, **Oliver Blankenstein⁴**, **Richard J Ross⁷** and **Charlotte Kloft¹**

¹Department of Clinical Pharmacy and Biochemistry, Institute of Pharmacy, Freie Universität Berlin, Berlin, Germany, ²Graduate Research Training Program, PharMetX, Berlin, Germany, ³Department of Pharmaceutical Technology and Chemistry, School of Pharmacy and Nutrition, Universidad de Navarra, Pamplona, Spain, ⁴Charité-Universitätsmedizin, Berlin, Germany, ⁵Diurnal Limited, Cardiff, UK, ⁶Institute of Mathematics, Universität Potsdam, Germany, and ⁷University of Sheffield, Sheffield, UK

Correspondence should be addressed to C Kloft

Email
charlotte.kloft@fu-berlin.de

We were delighted to see the letter to the editor by Sarafoglou *et al.* (1). The authors highlight important points made in our recent paper on paediatric population pharmacokinetic modelling to assess hydrocortisone replacement dosing regimens in young congenital adrenal hyperplasia (CAH) patients (2).

We acknowledge that extemporaneously compounded hydrocortisone suspensions from specific pharmacies can provide adequate replacement therapy as referenced by Sarafoglou *et al.* (3, 4). However, as discussed by Sarafoglou, extemporaneously compounded drugs are not subject to the same quality control measures as commercial medications licensed by the US Food and Drug Administration (FDA), which can lead to inconsistent quality between different compounding pharmacies or between batches, and varied results in patients with some patients becoming Cushingoid and some adrenally insufficient (5). In the United States of America (US), there has been little innovation in hydrocortisone therapies for the treatment of CAH over the last 60 years and, currently, there is still no licenced paediatric-specific preparation of hydrocortisone in the US. We acknowledge that in our, Europe-focussed study, this was not referenced.

Lastly, we agree that there is a need for new biomarkers to guide hydrocortisone replacement in CAH to optimise long-term health. In healthy children, considerable

interindividual variability in cortisol concentrations exists and in CAH patients, there is variability in response to hydrocortisone replacement therapy. Therefore, we agree that the measurement of cortisol alone is not sufficient to optimise therapy, especially as the current treatment does not replicate the physiological circadian rhythm of cortisol, and so measuring cortisol exposure does not take in to account the impact of unphysiological maximum and minimum concentrations of cortisol replacement therapy. As Sarafoglou *et al.*, suggest, future research is required to determine the biomarkers that in the short term will allow optimisation of hydrocortisone replacement therapy in CAH to improve long-term health outcomes.

In conclusion, both new, easy-to-administer paediatric hydrocortisone formulations with low dose strengths and the consideration of pharmacodynamics biomarkers are avenues that should be investigated further in both Europe and the US to reach the aim of effectively treating our young CAH patients with paediatric appropriate medication.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this letter.

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