Long-term follow-up of safety and disease control for hydrocortisone granules designed to give age-appropriate dosing with taste masking to children with adrenal insufficiency

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Context: Alkindi® (Hydrocortisone granules in capsules for opening), was developed by Diurnal Ltd., a pharmaceutical company developing endocrine products, and was recently licensed for oral administration to children with adrenal insufficiency (AI) from birth to 18 years. Previously, children received pharmacy compounded capsules to achieve age appropriate dosing, however almost 25% of batches were out of specification for mass and content uniformity and clinically evident under- and over-dosing was reported.

Conclusions: Alkindi® is a newly developed paediatric and neonatal formulation of immediate release hydrocortisone that is provided in appropriate unit dosage (0.5, 1 mg, 2 mg and 5 mg). Alkindi® was well tolerated with neither adrenal crisis nor AEs reported related to Alkindi® treatment. The most frequently reported AEs were infections, which were managed appropriately using sick day rules. There was no indication of either under-treatment or over-treatment, which is important for achievement of disease control in the growing child.

Patients and study design:

Open label, long term follow up, single centre study.

24 children completed the Alkindi® Phase 3 trial

→ **6 children or parents not willing for a further study**

18 children enrolled in this extension study

→ **6 children withdrew early by „withdrawal of consent“ mainly due to problems with taking the late night dose during the sleep**

12 children finished this extension study. Last patient last visit – 10th Aug 2018

Demographics:

	Cohort 1	Cohort 2	Cohort 3
n	9	6	3
Male/female	5/4	4/2	1/2
diagnoses	9 - CAH	5 – CAH 1 - Hypopituitarism	3 - CAH
Median ages at entry	1316 days (~3 years, 7 months	747 days (~ 2 years)	46 days
Mean duration of treatment (until 22nd Mar 2018)	326 days (~ 1 year)	635 days (~1.7 years)	719 days (~2 years)
Finishing study and continuing therapy after commercial supply	n=4	n=5	n=3

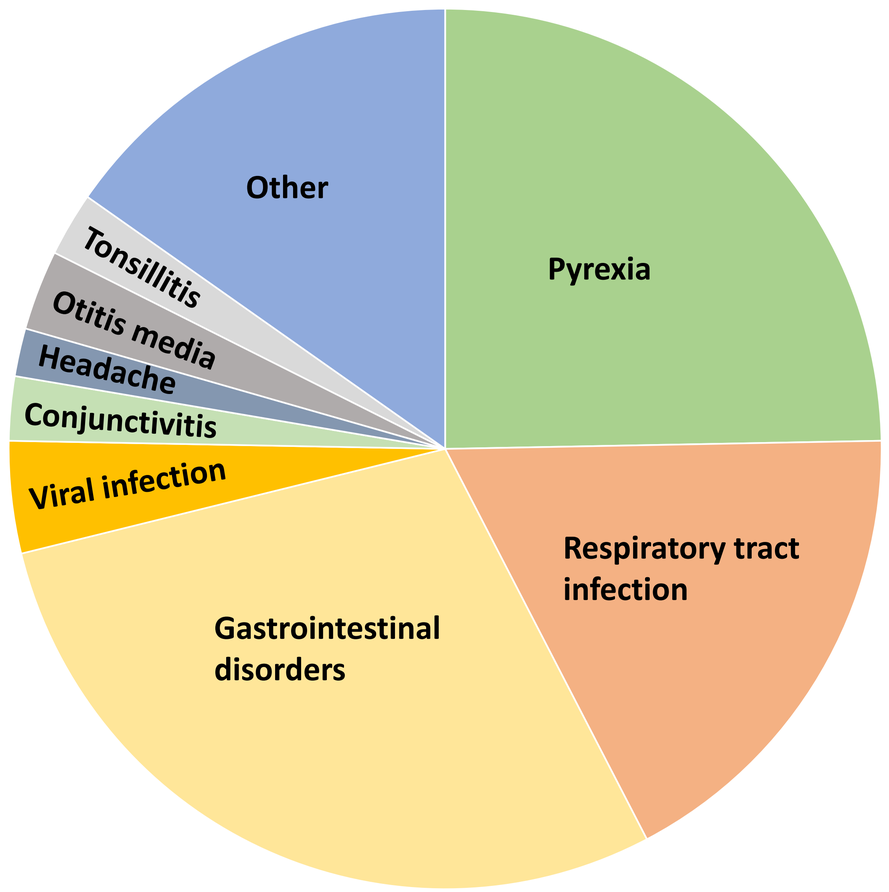
Results (last interim analysis – 22nd Mar 2018):

Overall mean daily dose ranged from 6.01 to 8.51 mg (10.4-12.0 mg/m² BSA) administered according to usual clinical practice (3x/day).

No changes in vital signs occurred that indicated an adverse effect of Alkindi®, no trends for accelerated or reduced growth (Z-scores).

Adverse events:

A total of 170 treatment-emergent adverse events (TEAEs) were recorded in 14 subjects (77.8%) overall.



No deaths, severe TEAEs, TEAEs leading to withdrawal from the study, and no TEAEs with a suspected causal relationship to Alkindi®.

Severe adverse events:

Eight SAEs occurred in 3 patients, not related to Alkindi®. No cases of adrenal crisis, no AEs of choking.

Gastroenteritis (n=4)	Vomiting (n=2)	Erysipelas (n=1)	Urinary tract infection (n=1)

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References: Neumann, Whitaker et al., Clinical Endocrinology 2018;88:21–29

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