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**OR23-05**

Injected depot formulations of somatostatin peptide analogs are routinely used to treat acromegaly and neuroendocrine tumors (NETs). CRN00808, a small molecule nonpeptide selective somatostatin receptor 2 (sst2) agonist, is being evaluated for efficacy and safety in patients with acromegaly. The current Phase 1 study was conducted in two Parts: In Part A, the absorption, metabolism, excretion, and mass balance of a single oral dose of 20 mg [$^{14}$C]-CRN00808 (3.0 MBq) oral solution was characterized in six healthy male subjects. Plasma, blood, urine, and feces were collected for up to 432 hours, and were analyzed for total radioactivity and CRN00808 concentrations (plasma only). Metabolite profiling was conducted on the plasma, urine, and feces samples. In Part B, the absolute bioavailability of CRN00808 was determined by administering a single oral dose of 20 mg CRN00808 compared with a single micro-tracer intravenous (IV) bolus injection of 50 μg [$^{14}$C]-CRN00808 (0.0185 MBq) in five healthy male subjects. The IV dose was administered approximately 90 minutes after the oral dose. Plasma samples were collected for up to 144 hours and were analyzed for total radioactivity and CRN00808 concentrations (plasma only).

Key data from Part A and Part B will be presented. Available data from Part A of the study show that >90% of radioactivity was recovered within 7 days of dosing. The primary route of excretion was the feces (>90%) with minimal excretion in the urine (<10%). Absorption of total [$^{14}$C]-CRN00808-derived radioactivity in plasma was rapid (median $T_{max}$=1 hour), and the mean $C_{max}$, $AUC_{0-\infty}$, and $t_{1/2}$ were determined to be 194 ng-equivalents/mL, 3340 ng-equivalents.hr/mL, and 31 hours, respectively. The pharmacokinetic parameters of unchanged CRN00808 in plasma were similar, suggesting that majority of the circulating drug-derived radioactivity is accounted for by unchanged CRN00808 and there are no abundant circulating metabolites. Treatment emergent adverse events associated with CRN00808 were generally mild and transient, and consistent with those reported with other somatostatin agonists. In conclusion, results from this clinical trial in healthy volunteers confirm that CRN00808 has excellent drug-like properties for chronic once-daily oral treatment of patients with acromegaly.

# Adrenal

## ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

### *Inhaled Corticosteroids and Adrenal Insufficiency: A Meta-Analysis and Systematic Review*

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**MON-154**

Inhaled corticosteroids have been associated with adrenal insufficiency in adult and pediatric populations[1,2]. When inhaled corticosteroids are absorbed orally, they can have a systemic effect. Corticosteroid type, particle size, delivery method, liver metabolism via CYP 3A4, protein binding, and half-life all impact the magnitude of the systemic effect of inhaled corticosteroids[3]. We conducted a systematic review and meta-analysis in order to establish the prevalence of adrenal insufficiency among adult patients taking inhaled corticosteroids. We searched the PubMed, Embase and Cochrane databases for "adrenal insufficiency" AND "inhaled corticosteroids", yielding 318 search results. We also hand-searched the references of relevant articles. In total, 30 studies were included in our meta-analysis. Amongst these, 15 studies were RCTs and 13 studies were cross-sectional studies. All of these studies used ACTH stimulation testing to diagnose adrenal insufficiency. Risk of bias assessment was completed for all studies using the Cochrane risk of bias assessment tool. Patients with asthma were the population examined in 90% of the included studies. Prevalence of adrenal insufficiency demonstrated by ACTH stimulation testing varied from under 5% to up to 55% among different studies. We recommend that further studies carefully examine and report the clinical impact of abnormal ACTH stimulation testing results, the concomitant use of oral corticosteroids, and the impact of the inhaled corticosteroid delivery method, the corticosteroid type, the corticosteroid dosage, and the duration of therapy.

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# Pediatric Endocrinology

## PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY

### *Incidentally Found Severe Hypercalcemia in a Pediatric Patient, Diagnostic Challenge*

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**SUN-096**

**Introduction:** Idiopathic infantile hypercalcemia is an intriguing feature of Williams syndrome (WS), occurring in ~15% of diagnoses and is typically not clinically severe. Symptomatic hypercalcemia usually resolves during childhood, but lifelong abnormalities of calcium(Ca) and vitamin D metabolism may persist. The cause of the abnormality in Ca metabolism is still unknown. Hypercalciuria generally accompanies hypercalcemia, but isolated hypercalciuria, especially after infancy, can also occur. Nephrocalcinosis is relatively rare, found in less than 10% of patients undergoing renal ultrasonography. We report a 13-month-old female infant with a history of peripheral pulmonary stenosis and constipation, who presented with severe hypercalcemia that led to a new diagnosis of WS. **Case presentation:** A 13-month-old girl with a history of peripheral