Clinical case: 62 years old woman with unremarkable thyroid history presented with chronic mid-chest pain and dysphagia in 2016 found to have a mass in middle third of esophagus. Biopsies revealed invasive squamous cell carcinoma (T3N0). She underwent radiotherapy and esophagectomy.
On 1/2018, surveillance imaging detected a new tracheobronchial angle lymph node, which was confirmed as hypermetabolic and likely malignant by PET scan. Patient received additional 5 cycles of radiotherapy followed with 5 cycles of chemotherapy with Oxaliplatin and Capecitabine. Since post-chemotherapy PET scan showed local recurrence, patient was started on PD1 inhibitor, Pembrolizumab 200 mg Q3 week. After 3 doses patient developed cold intolerance, weight gain and low mood. Her TSH was 173 uIU/ml (0.27-0.42), FT4 <0.1 ng/dL (0.9-1.8) and referred to endocrine clinic. Repeat TSH was 190 uIU/ml, FT4 0.2 ng/dL, TPOAbs 619 IU/ml (<35) and TSI<0.1 IU/L (<0.55). Adrenal insufficiency was ruled out and started on levothyroxine 50 mcg in the morning, increased to 75 mcg. After 2 months of levothyroxine use, TSH was 11.8 uIU/ml and FT4 1.3. Pembrolizumab therapy is restarted shortly after.
Conclusion: National Comprehensive Cancer Network guideline for management of immunotherapy related toxicities recommends routine monitoring of TSH and FT4 at baseline and every 4-6 weeks during immunotherapy, follow up every 12 weeks and TPO antibodies if TSH is high. This patient's clinical symptoms of hypothyroidism might be confused by nonspecific symptoms of underlying malignancy. Combination radiotherapy and immunotherapy place this patient at higher risk of developing hypothyroidism. This case showed the successful collaboration of endocrinology and oncology team in giving vulnerable patient an optimized care with good clinical outcome.
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Tumor Biology

TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS

Phase Ib Study of Dual Therapy with an Aromatase Inhibitor Exemestane and Carboplatin-Based Therapy for Postmenopausal Women with Advanced Non-Small Cell Lung Cancer

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SUN-125

Objectives: Estrogen receptors (ER-alpha, ER-beta) and aromatase (key enzyme for estrogen synthesis) are expressed in most human non-small cell lung cancers (NSCLCs). High intratumoral estrogens and elevated aromatase in NSCLC are reported to predict poor clinical outcome. *In vitro,* estrogen stimulates NSCLC gene expression and, tumor progression and diminishes tumor cell apoptosis. Furthermore, preclinical NSCLC models demonstrate that aromatase inhibitors (AIs) prevent these processes, and that cisplatin with AIs elicits dramatic growth inhibition. Additionally, depletion of autocrine/paracrine estrogen production hypersensitizes cells to DNA-damaging effects of platinum therapy, providing a rationale for this trial. This open-label, phase 1b, single-center study evaluated safety and tolerability of AI exemestane combined with carboplatin and pemetrexed in postmenopausal women with stage IV non-squamous, NSCLC.
Materials/Methods: Exclusion criteria included untreated CNS metastasis, major surgery in prior 4-weeks to therapy, prior/concurrent investigational or standard therapy (except TKI and/or immunotherapy in prior 4-weeks). Trial patients received escalating doses of exemestane (starting 1-week before chemotherapy) at 25 mg PO daily (Cohort 1) or 50 mg PO daily (Cohort 2) with carboplatin (AUC 6 mg x min/mL) and pemetrexed (500 mg/m2) IV q3 weeks for 4 cycles. Thereafter, patients could continue therapy with exemestane and/or pemetrexed.
Result: Ten patients consented for study and 2 patients screen-failed. Three patients completed therapy in Cohort 1, and five patients were treated in Cohort 2. The median number of cycles was 15 (range 1-54). The MTD was exemestane 50 mg PO daily with combination chemotherapy. Intention to treat analysis showed an overall response rate (ORR) of 62.5% [5 of 8 patients with partial remission (PR)] and clinical benefit rate was 87.5% (7 of 8 patients with stable disease or PR). ORR was significantly associated with tumor aromatase expression (p=0.02). There was no correlation between ORR and ER-alpha or progesterone receptor by IHC. Circulating estrogen levels decreased with exemestane, and quality of life measures did not significantly change. No patients left the study for adverse events.
Conclusion: CCombination chemotherapy with exemestane in postmenopausal women with Stage IV non-squamous, NSCLC is safe and well-tolerated. Biomarker studies show that ORR correlates significantly with tumor aromatase expression. These findings support future clinical trials to confirm antitumor efficacy with this combination therapy.

Neuroendocrinology and Pituitary

PITUITARY TUMORS: TRIALS AND STUDIES

Human Absorption, Metabolism, Excretion, and Absolute Oral Bioavailability of ^{14}C-CRN00808, an Orally Bioavailable, Nonpeptide, Selective, Somatostatin Receptor 2 (sST2) Biased Agonist for the Treatment of Acromegaly

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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