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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