Neuroendocrinology and Pituitary

PITUITARY TUMORS II

Prior Injectable Somatostatin Receptor Ligand Dose Does Not Predict Oral Octreotide Response In The Treatment Of Acromegaly: Results From The Phase 3 OPTIMAL Study

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Background: Injectable somatostatin receptor ligands (SRLs) are the most widely used therapy to control acromegaly. Oral octreotide capsules have been formulated as a potential therapy for this disorder and the efficacy and safety was evaluated in the CHIASMA OPTIMAL prospective phase 3 study in patients with acromegaly who were controlled on injectable SRL treatment of varying doses (Samson et al. ENDO 2020). **Methods:** Patients with confirmed acromegaly, who had been receiving a stable dose of injectable SRL (≥3 months) up until study entry, were randomized to receive octreotide capsules (40 mg/day) or placebo for 36 weeks. Patients were dose titrated to 60 or 80 mg of oral octreotide or equivalent placebo through week 24 at the investigator's discretion based on increase of IGF-I levels or worsening of acromegaly signs and symptoms. The primary efficacy endpoint was the proportion of patients who maintained their biochemical response at the end of 36 weeks, defined as average IGF-I ≤1 x ULN between Weeks 34 and 36. An analysis evaluated maintenance of response based on prior dose of injectable SRL. Prior doses of injectable SRL were categorized based on the following classifications: octreotide 10 mg every 4 weeks or lanreotide 60 mg every 4 weeks or 120 mg every 8 weeks were stratified as low; octreotide 20 mg every 4 weeks or lanreotide 90 mg every 4 weeks or 120 mg every 6 weeks were stratified as medium; octreotide 30 mg or 40 mg or lanreotide 120 mg every 4 weeks were stratified as high. Randomization was stratified based on low dose vs med/high dose and efficacy results compared for these strata. The response rates reported for the primary end point are slightly adjusted for stratification differences as prespecified in the statistical analysis plan. **Results:** Six patients (21.4%) in the octreotide capsule group had received prior treatment with low doses of injectable SRLs while 22 (78.6%) had received prior treatment with medium-high doses of injectable SRLs. Maintenance of response was observed in 16 patients receiving oral octreotide. This included 66.7% of patients (n=4) previously receiving low doses of injected SRLs and 54.5% of patients (n=12) on medium-high injected doses. The treatment effect was consistent irrespective of prior dose of injectable SRL (odds ratio: 5.4 in low dose and 5.9 in medium-high dose). **Conclusion:** The CHIASMA OPTIMAL study recruited a population receiving predominantly medium-high doses of injectable SRLs and demonstrated maintenance of response in 58% of patients. Oral octreotide treatment effect was consistent irrespective of prior dose of injectable SRL.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS III

Amphotericin B Induced Hypocalcemia in a Patient With Severe Hypercalcemia Due to Acute T-Cell Leukemia/Lymphoma

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Abstract: Adult T-cell Leukemia/lymphoma (ATL) is a rare and aggressive type of non-Hodgkin's lymphoma. Patients with ATL commonly develop severe hypercalcemia leading to life-threatening complications like acute kidney injury, cardiac arrhythmias, altered mental status, and coma. The treatment of hypercalcemia of malignancy is often challenging. Here we present a case of ATL with severe hypercalcemia who was treated prophylactically with amphotericin B, leading to a significant and rapid drop in the calcium levels into the hypocalcemia range. We discussed the possible mechanism that leads to the rapid decline in the calcium levels in this patient. **Introduction:**Adult T-cell Leukemia/lymphoma (ATL) is a malignancy that develops from mature T-lymphocytes. It is a rare and highly aggressive type of non-Hodgkin's lymphoma. The incidence of ATL is reported to be high in endemic areas like Japan, south and Central America, Caribbean islands, and Florida state of the United States. Fortunately, the incidence of ATL is about 0.05 cases per hundred thousand people in the United States, which is very low [1]. There is a strong association between human T-lymphotropic virus type 1 (HTLV-1) and ATL, with HTLV-1 genome detectable in 100 percent of tumor clones of ATL [2]. However, the percentage of HTLV-1 carriers that develop ATL is minuscule. ATL is clinically divided into four clinical subtypes (acute, lymphomatous, chronic and smoldering types) with acute and lymphomatous subtypes having a very poor prognosis, median survival despite aggressive regimens being just 7.7 months [3]. Immunodeficiency, hypercalcemia (≥10.8 milligrams per deciliter) and tumor lysis syndrome are common complications of ATL as with many other malignancies. Along with aggressive chemotherapy regimens, the primary malignancy itself causes severe immunodeficiency and puts the patient at a very high risk of developing opportunistic infections [4]. Hence these patients will be needing antibiotic prophylaxis and antifungal prophylaxis during the chemo regimen and are often treated with multiple antibiotics and antifungals during the course of the disease. One such anti-fungal agent is amphotericin B, primarily used to treat aggressive and systemic fungal infections.Amphotericin B targets the fungal cell wall by binding to the ergosterol molecule in it and forms pores that