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Erdheim-Chester disease: Case report with multisystem manifestations

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A 61-year-old man presented with a 3-year history of extensive yellow plaques on both eyelids. The patient also reported retro-orbital headache, lower limb pain, polydipsia-polyuria and progressive fatigue, since last year. Reflectance confocal microscopy showed clusters of multinucleated roundish structures, along with discoid-shaped structures, at superficial dermis. Histopathology examination proved them to be Touton cells and foamy histiocytes respectively. Immunohistochemically, foamy histiocytes were positive for CD68 and negative for S-100 and CD1a. Further investigation revealed retro-orbital masses, osteosclerosis of the distal long bones, pleural and pericardial effusion, diabetes insipidus and retroperitoneal fibrosis. Therefore, the patient was diagnosed with Erdheim-Chester disease. A BRAF V600E mutation was confirmed and vemurafenib (1920 mg/day) was initiated. However, three weeks later the patient developed DRESS syndrome and the treatment was stopped. After multidisciplinary discussion, it was decided to begin treatment with cobimetinib (40 mg/day). A clinically and radiographically (assessed with 18F-FDG PET) significant improvement was noted after three months of therapy. Erdheim-Chester disease is a non-Langerhans cell histiocytosis with possible cutaneous involvement. Diagnosis is challenging and should be suspected in the presence of xanthelasma-like lesions and signs of a multisystem disease. Since 2012 with discovery of BRAF mutations in about 50% of patients, BRAF inhibitors have become a first-line treatment. More recently, cobimetinib, a MEK inhibitor, has been used in patients with BRAF wild-type disease, or in who cannot tolerate or do not respond to vemurafenib. To the best of our knowledge, we report herein the first case of Erdheim-Chester disease evaluated by confocal microscopy.

Commercial disclosure: None identified.

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Long-term safety of apremilast treatment in patients with psoriasis or psoriatic arthritis: Pooled analysis for 260 weeks and beyond in the ESTEEM 1 and 2 and PALACE 1-4 phase 3 trials

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Background: Apremilast 30 mg bid (APR) safety and tolerability were evaluated in patients with moderate to severe plaque psoriasis (ESTEEM 1 and 2) or active psoriatic arthritis (PALACE 1-4). We report findings from a pooled analysis of these 6 studies.

Methods: Safety findings are reported for placebo-controlled (0-16 weeks in ESTEEM 1 and 2 or 24 weeks in PALACE 1-4) and overall APR-exposure (0 to ≥260 weeks, through December 2017) periods.

Results: A total of 2593 patients were included in the weeks 0-16/24 safety analysis (placebo, n = 1089; APR, n = 1504); 2157 patients received APR for 0-≥ 260 weeks, and 243 patients had ≥ 260 weeks of APR exposure. With placebo vs APR, low and comparable rates of severe (3.7% vs 4.4%) and serious (3.2% vs 2.5%) adverse events (AEs) were observed during the placebo-controlled period. The most common AEs (≥5%) with APR during the placebo-controlled period were nausea (16.4%), diarrhea (15.6%), headache (7.9%), URTI (7.1%), and nasopharyngitis (5.7%). During the full APR-exposure period (0 to ≥260 weeks, 5163.1 patient-years), incidence of AEs, severe AEs, serious AEs, and AEs leading to withdrawal did not increase with increasing cumulative exposure. Exposure-adjusted incidence rates/100 patient-years were comparable for placebo vs APR for MACE (7.0 vs 7.0), malignancies (1.5 vs 1.3), opportunistic infections (3.8 vs 1.3), suicide/self-injury (0.3 vs 0.2), and depression (2.0 vs 3.3) during the placebo-controlled period and remained low with prolonged APR exposure.

Conclusions: No new safety signals were observed with APR exposure ≥5 years in clinical studies of patients with psoriasis or psoriatic arthritis.

Commercial disclosure: This study was sponsored by Celgene Corporation.

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Effect of concomitant common cardiovascular medications on efficacy of sonidegib 200 mg daily in patients with locally advanced basal cell carcinoma: Results of the 42-month randomized, double-blind BOLT study

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Introduction: Sonidegib, a hedgehog pathway inhibitor, is approved for treatment of locally advanced basal cell carcinoma (laBCC) not amenable to surgery or radiotherapy. This post hoc analysis of the pivotal BOLT studyincluded objective response rate (ORR) and duration of response (DOR) per investigator review in laBCC patients taking concomitant common cardiovascular (CV) medications.

Methods: BOLT was a randomized, double-blind, multicenter phase 2 study; patients were randomized 1:2 to sonidegib 200 or 800 mg orally qd, respectively. Tumor responses were assessed using modified Response Evaluation Criteria in Solid Tumors for laBCC. Safety assessments included adverse event (AE) monitoring.

Results: At 42 months, laBCC patients receiving sonidegib 200 mg qd (n = 66) achieved overall ORR (95% confidence interval [CI]) of 71.2% (58.7%-81.7%) by investigator review. In patients taking concomitant CV medications, ORR (95% CI) was 66.7% (9.4%-99.2%) for angiotensin II antagonists (n = 3), 92.3% (64.0%-99.8%) for angiotensin converting enzyme inhibitors (ACEI; n = 13), 75.0% (19.4%-99.4%) for direct thrombin inhibitors (n = 4), and 77.8% (40.0%-97.2%) for statins (n = 9). Overall median (95% CI) DOR per investigator review was 15.7% (12.0%-20.2%) for laBCC patients. Median DOR (months, 95% CI) was 11.1 (5.7-13.6) for statins; 19.4 (not estimable [NE]) for ACEI; 13.6 (NE) for direct thrombin inhibitors; and NE for angiotensin II antagonists. Overall, 97.5% patients receiving sonidegib 200 mg qd experienced an AE; of those 55.8% experienced a grade 1-2 AE.

Conclusions: Concomitant common CV medications had no impact on efficacy in laBCC patients receiving sonidegib 200 mg qd.

Commercial disclosure: Writing and editorial support were provided by Ginny Feltzin, PhD, of AlphaBioCom, and funded by Sun Pharmaceutical Industries, Princeton, New Jersey.

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Spiradenoma arising in the breast of a high-risk breast cancer patient and review of cases over 76 years

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Spiradenomas stem from eccrine and apocrine glands to form benign tumors. When arising on the breast, nipple, and areola region, spiradenomas can be difficult to differentiate from more worrisome breast masses in patients with a prior history of breast cancer. These cutaneous tumors can be mimicked by a range of adnexal growths and play a role in syndromic conditions. We present a case of a 56-year-old woman with a 20-year slowly enlarging left lower inner quadrant breast mass reviewed on mammography in a high-risk breast cancer patient, which was later excised and diagnosed as a spiradenoma. Spiradenomas can be challenging to diagnose as they can present with similar findings on inexpensive and noninvasive testing. While biopsy is the definitive tool for diagnosis, this is contraindicated in mimickers such as epidermal cysts. To our knowledge, there are only six case reports of breast spiradenomas. We have reviewed the histopathology of this case including stains with periodic acid—Schiff cytokine 5/6 immunohistochemical stain (IHC) carcinoembryonic antigen (CEA) and epithelial membrane antigen IHC, P63 IHC, gross cystic disease fluid protein 15 (GCDFP-15) IHC, and endoplasmic reticulum IHC and summarized all cases of breast spiradenomas and their malignant counterpart spiradenocarcinomas available in the literature over the past 76 years compiling their presentations, histopathologic stains, and imaging findings.

Commercial disclosure: None identified.