PCN1

BONE SAFETY PROFILE OF DENOSUMAB THERAPY: A PHARMACOVIGILANCE CHARACTERIZATION ANALYSIS

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OBJECTIVES: Denosumab is a biologic approved in June 2010 to treat bone tumors and hypercalcemia of malignancy. This study characterizes bone-related safety signals of subcutaneous atypical femoral fractures (SAF) and osteonecrosis of the jaw (ONJ) in relation to denosumab therapy. METHODS: The FDA Adverse Event Reporting System (AERS) was used to detect signals associated with denosumab therapy. Denosumab event reports submitted between July 1, 2006 and December 31, 2013 were retrieved and disproportionality reporting of SAF and ONJ was calculated.

RESULTS: A total of 26,216 adverse event reports submitted for denosumab during the analysis period, corresponding to 30 for SAF and 721 for ONJ. Denosumab was significantly associated with more than expected reporting of SAF (EBGM =17.5, 95%CI=9-67.0) and ONJ (EBGM =26.9, 95%CI=21-36.9) compared to other drugs. The majority of denosumab users who experienced both events were females, and average age was 69 years (SAF SD=9.5, ONJ SD=11.3). 12 SAF and 65 ONJ events lead to hospitalization. 45 and 14 ONJ events are attributed to patient disability and death, respectively. Other factors could have lead to these serious outcomes, including comedinations and comorbidities.

CONCLUSIONS: SAF and ONJ are potential risks of denosumab therapy. Patients with thigh or hip pain should seek immediate medical help, and periodic dental and maxillofacial evaluations should be performed before and during denosumab therapy. Pharmacoepidemiologic studies are recommended to further characterize these risks, as some patients were treated with other medications, including systemic corticosteroids at the time of event occurrence.

PCN2

META-ANALYSIS OF THE SAFETY OF SIPULUCEL-T IMMUNOTHERAPY IN PROSTATE CANCER

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OBJECTIVES: Sipuleucel-T is an autologous active cellular immunotherapy designed to reduce the risk of death in patients with prostate cancer. The aim of this study was to evaluate the safety of Sipuleucel-T for patients with prostate cancer. METHODS: PubMed, EMBASE and the Cochrane Central Register of Controlled Trials were searched through January 10, 2015. Criteria for inclusion were randomized, placebo-controlled clinical trials on Sipuleucel-T, patients receiving three infusions, 36 months follow-up and the availability of outcomes data for adverse events. The primary outcome was the total number of adverse events. Secondary outcomes were examined eighteen specified adverse events. Two investigators selected studies independently and assessed the quality of studies using the Jadad scale. Point estimate with a 95% confidence interval were presented. Fixed-effects or random-effects models were based on the evaluation of heterogeneity.

RESULTS: Five clinical trials encompassing 1031 patients were included. The overall adverse events rate was 1.02 (95% CI 1.00-1.03). The most frequent reported outcomes, differences were detected between Sipuleucel-T and placebo on chills (RR = 1.14; 95% CI 1.14-1.52), dyspnea (RR = 1.32; 95% CI 1.22 to 1.43), nausea (RR = 1.96; 95% CI 1.04-3.85) and dyspepsia (RR = 2.72; 95% CI 1.34 to 10.36, p=0.012, 350 patients). CONCLUSIONS: Sipuleucel-T significantly increased the risk of selected adverse events in patients with prostate cancer. Although many adverse events were transient, patients and providers should consider the potential risk of treatment with Sipuleucel-T.

PCN3

TREATMENT FOR CHEMOTHERAPY-RELATED COGNITIVE DYSFUNCTION: REVIEW OF THE LITERATURE

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OBJECTIVES: Chemotherapy-related cognitive dysfunction (CRCD), colloquially known as ‘chemo fog’ or ‘chemo brain,’ describes the impact of chemotherapy on cognitive functioning in domains ranging from memory to expressive language. CRCD is generally described as direct or indirect effects of chemotherapy on the central nervous system, may occur at some level of intensity in as many as 75% of patients who have undergone chemotherapy, and impacts quality of life, educational/occupational success and social functioning. Management of CRCD includes both pharmacological and non-pharmacological therapies. METHODS: To better understand the range of treatments that have been studied for CRCD, and their relative efficacy, a comprehensive review of the published literature was undertaken. A MEDLINE search of the literature was conducted for relevant sources published in English between January 2005 and December 2014. The search was limited to studies describing trials of interventions to manage or treat CRCD using non-pharmacological interventions.

RESULTS: Of 162 records retrieved, 11 described interventions targeting CRCD. Pharmacological therapies used included erythropoietin, dexmethylphenidate, gabapentin, and pyragnol. Half of the studies focused on breast cancer. Most resulted in small decrements in significant findings, but two studies of erythropoietin in patients with prostate cancer had high risk of selection bias and indirectness. All trials had high risk of directness, and 2) identify if any racial/ethnicity differences accounted for the association between diabetes and pancreatic cancer. The aims of this study were to 3) assess whether diabetes is associated with pancreatic cancer in the elderly Medicare population,