[LB-1167] Fracture Risk after Stopping Adjuvant Denosumab in Hormone Receptor Positive Breast Cancer Patients on Aromatase Inhibitor Therapy – an Analysis of 3,425 Postmenopausal Patients in the Phase III ABCSG-18 trial

Georg Pfeiler, Medical University of Vienna/ Department of Obstetrics and Gynecology and Comprehensive Cancer Center

October 1, 11:51 AM - 12:00 PM
Room 517 A/Palais des congrès de Montréal

Session: Late-Breaking Concurrent Orals: Clinical

Abstract

Fracture Risk after Stopping Adjuvant Denosumab in Hormone Receptor Positive Breast Cancer Patients on Aromatase Inhibitor Therapy – an Analysis of 3,425 Postmenopausal Patients in the Phase III ABCSG-18 trial

Author(s)

Georg Pfeiler, Guenther G. Steger, Daniel Egle, Richard Greil, Florian Fitzal, Viktor Wette, Marija Balic, Ferdinand Haslbauer, Elisabeth Melbinger-Zeinitzer, Vesna Bjelic-Radisic, Jonas Bergh, Raimund Jakesz, Christian Marth, Paul Sevelda, Brigitte Mlineritsch, Ruth Exner, Christian Fesl, Sophie Frantal, Christian F Singer, Michael Gnant

Background: Endocrine therapy with aromatase inhibitors (AI) for at least 5 years is standard of care in patients with early hormone receptor (HR+) positive breast cancer. ABCSG-18 has shown (1) a high fracture risk in patients on AI treatment, (2) a significant reduction of clinical and vertebral fractures by 6-monthly denosumab (HR=0.5, p<0.0001, Lancet 2015). Recent reports indicate an elevated risk of rebound-associated fractures - especially multiple vertebral fractures - after stopping denosumab. Here we present data on fracture risk >6 months after the last dose of denosumab or placebo for patients with HR+ early breast cancer.

Methods: In the prospective, double-blind, placebo-controlled phase III ABCSG-18 trial, 3,425 postmenopausal HR+ patients treated with adjuvant AI were enrolled to denosumab 60mg or placebo s.c. q6 months until the prespecified number of 247 first clinical fractures was reached. All patients received at least 2 doses of denosumab (median: 7 doses), the primary trial endpoint was time to first clinical fracture risk.

Results: 2,451 patients stopped AI later than 6 months after the last dose of denosumab/placebo. 387 patients ended their AI intake prior to, and 295 patients within 6 months after the last dose of denosumab/placebo. During a median off-treatment follow-up of 36 months, 318 fractures in 199 patients (subject incidence rate 6.2%) have occurred. No difference in overall fracture risk in patients who stopped denosumab compared to patients who stopped placebo could be detected (163 vs 155 fractures in 98 vs 101 patients, time to first fracture: HR 0.92 (0.70,1.22)). However, when looking specifically at clinical fractures, patients who stopped denosumab had a significantly higher risk of clinical vertebral fractures and multiple clinical vertebral fractures compared to patients who stopped placebo (39vs14 fractures in 22vs9 patients, HR 2.44 (1.12,5.32); 28vs8 fractures in 11vs3 patients, HR 3.52 (0.98,12.64)). This increased risk of clinical vertebral as well as multiple clinical vertebral fractures in patients who stopped denosumab, only occurred in patients who ended AI treatment prior to or >6 months after the last dose of denosumab/placebo, whereas no difference was seen in patients who ended AI treatment within 6 months of stopping denosumab/placebo.

Conclusion: Rebound-associated fractures after termination of adjuvant denosumab therapy may be avoided when stopping bone-compromising AI therapy within 6 months.

Disclosures:
Georg Pfeiler: Novartis, Pfizer, AstraZeneca #100; Amgen #101