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File: ■ Boswellia (*Boswellia serrata*, Burseraceae) Cream ■ Radiotherapy-induced Skin Damage

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RE: Boswellia-based Cream Improves Radiation-induced Erythema in Patients Undergoing Postsurgical Treatment for Breast Cancer

Togni S, Maramaldi G, Bonetta A, Giacomelli L, Di Pierro F. Clinical evaluation of safety and efficacy of *Boswellia*-based cream for prevention of adjuvant radiotherapy skin damage in mammary carcinoma: a randomized placebo controlled trial. *Eur Rev Med Pharmacol Sci*. 2015;19(8):1338-1344.

Among the most common adverse side effects from radiation therapy for breast cancer are acute radiation erythema and other skin reactions. Such adverse side effects can affect a patient's quality of life and potentially disrupt the therapeutic program. A radiation-induced skin injury is a complex wound, with direct tissue damage mediated by a sharp increase of free radicals, resulting in DNA damage and alteration of protein, lipids, and carbohydrates, and leading to inflammatory changes. No standard of care exists to prevent or control radiation-induced skin injury. Extracts of the resin of boswellia (*Boswellia serrata*, Burseraceae) with boswellic acids reportedly exert anti-inflammatory activities, reduce skin redness and irritation, and help soothe irritated skin when applied topically. These authors conducted a parallel-group, randomized, placebo-controlled trial to evaluate the safety and efficacy of the application of a base cream containing boswellic acids in the proprietary formulation Bosexil® (Indena S.p.A.; Milan, Italy) to prevent and relieve radiation-induced skin injury in patients receiving radiotherapy after surgery for breast cancer.

Bosexil is the Phytosome® form of the triterpenoid acid fraction from boswellia. It contains ≥25% total triterpene acids (boswellic and lupeolic acids) and ≥10% total β-boswellic acids. According to the manufacturer, Indena (http://www.phytosome.info), Phytosome is a proprietary technology that increases the absorption of ingredients, improving their systemic bioavailability.

For this study, 114 women undergoing adjuvant radiotherapy after breast cancer surgery were randomly assigned to treatment with boswellia cream 2% (n=55) or a placebo base cream (n=59). Contents of the placebo base cream were not described. The mean age of the patients was 58.2 ± 11.1 years (median, 58.5 years). Patients who received concomitant or previous chemotherapy totaled 17 (31%) in the boswellia group and 19

(32%) in the placebo group. All patients were overweight and had similar skin and iris pigmentation, phototype, and body mass index.

The authors report that radiation therapy was delivered with 2 tangential fields to the chest wall with a photon beam energy of 6 Mv; for large breasts, 4 fields with photon beam energy of 6 Mv and 18 Mv were delivered with differential weights. The prescribed dose was 2 Gy per fraction, with the target volume ranging from 95% to 107%. All measures, including photographic evaluations, were performed after the patients received a dose per breast of 50 Gy, usually reached after 5 weeks of treatment of 5 doses weekly.

On days of radiation therapy, the patients applied the cream twice daily, immediately after treatment and before bedtime. On days with no radiotherapy, they applied the cream in the morning and at night.

The boswellia cream was not always well tolerated, as some patients reported a non-absorbed residue. Its fragrance was perceived as pleasant by some and too intense by others.

Acute skin reactions were clinically evaluated by a visual grading scale (slight, moderate, and intense) and computer-assisted skin color analysis. Toxicity was measured on the Radiation Therapy Oncology Group (RTOG) rating scale, which ranges from no reaction (degree 0) to ulceration, hemorrhage, and necrosis (degree 4).

The primary endpoint was the intensity of erythema after reaching the 50 Gy radiation dose. More patients in the base cream group (49%) reported intense erythema than in the boswellia cream group (22%). Erythema intensity was reported as slight more often in the boswellia cream group (36.4%) than in the base cream group (20.3%). Moderate erythema was reported by more patients in the boswellia group (41.8%) than in the base cream group (30.5%). The most often reported (mode) intensity of erythema was intense (70.7%) in the base cream group and slight (62.5%) in the boswellia cream group. The differences measured in the grades of visual intensity of erythema were statistically significant (P=0.009).

The authors report trends of efficacy (P=0.018) between treatments when considering concomitant chemotherapy. For those not undergoing chemotherapy during the study, more patients treated with boswellia cream (50.0%) scored the intensity of erythema as slight than did patients in the base cream group (23.0%). In those same patients, intense erythema was reported by fewer in the boswellia cream group (19.0%) than in the base cream group (48.6%). For the patients receiving chemotherapy, fewer (29.0%) in the boswellia cream group reported intense erythema than in the base cream group (47.0%); the difference was not statistically significant.

A more objective method of assessing skin damage is based on the skin turning magenta-red or mauve in color in the advanced phase of erythema. Using this method, the authors determined by computer-assisted digitalization of magenta color in photographs that the mean value of skin damage was significantly lower in the boswellia cream group (10.1%) than in the base cream group (13.3%) (P=0.009).

Because topical hydrocortisone is used to prevent and treat radiation-induced dermatitis, the authors sought to determine if the use of hydrocortisone cream differed between the

2 groups. The percentage of patients in the boswellia cream group using cortisone (25.0%) was significantly lower than that of the base cream group using cortisone (63.0%) (P<0.0001).

The study's second endpoint was the toxicity of radiotherapy in the 2 groups. The treated skin area of each patient was examined with every 20 Gy delivered, unless additional evaluations were requested or if specific problems arose. Skin toxicity was determined to be RTOG degree 1 (follicular, faint or bright erythema, epilation, dry desquamation, decreased sweating) by 28.8% of those in the base cream group and by 45.5% of those in the boswellia cream group. More patients in the base cream group (71.2%) received a rating of RTOG degree 2 (tender or bright erythema, patchy moist desquamation, moderate edema) than in the boswellia cream group (45.6%). Those differences were close to statistical significance (P=0.066).

Adverse side effects totaled 29 in the base cream group and 21 in the boswellia cream group. A trend was observed toward a reduction of superficial symptoms such as itching and burning in the boswellia cream group (10.0%) compared with the base cream group (22.5%).

"Our investigation on patients with breast carcinoma undergoing radiotherapy showed that a base cream containing boswellic acids (boswellia cream) could be safely applied to prevent or alleviate radiation-induced skin reactions," conclude the authors.

Authors Togni and Maramaldi are employees of Indena S.p.A., manufacturer of Bosexil, and author Giacomelli is a consultant for the company.

—*Shari Henson*

Referenced article can be accessed at http://www.europeanreview.org/article/8795.