Nail Disorders in a Woman Treated with Ixabepilone for Metastatic Breast Cancer

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Abstract. Ixabepilone (Ix) (BMS-247550®) is a potent member of a new class of microtubule-stabilizing cytotoxic agents known as epothilones. In pre-clinical studies, Ix has shown anticancer activity against several cancer types, including paclitaxel-resistant models, both in vitro and in vivo. The major toxicities associated with Ix are myelosuppression, sensory neuropathy and neutropenia. Other minor side-effects include asthenia/fatigue, stomatitis, anorexia, alopecia, skin reaction, hypersensitivity reactions and a fluid-retention syndrome. Although Ix is functionally correlated to taxanes, no previous evidence exists regarding Ix-related nail disorders. Here, we report a case of a 59-year-old woman treated with Ix at 40 mg/m² day 1 q 21 days who, after 8 cycles of therapy, developed onycholysis and subungual hemorrhagic bullas in the fingernails.

Ixabepilone (Ix) (BMS-247550®) is a potent member of a new class of microtubule-stabilizing cytotoxic agents known as epothilones (1). Although structurally unrelated to the clinically validated taxanes, it acts similarly, by promoting the formation and stabilization of microtubules, arresting proliferating cells in mitosis and causing cell death by apoptosis. In pre-clinical studies, Ix has shown anticancer activity against several cancer types, including paclitaxel-resistant models, both in vitro and in vivo (1). Several phase II and III clinical trials with Ix are ongoing, and the use of this drug seems to be particularly indicated for taxane-pretreated breast cancer patients (2-5).

The major toxicities associated with Ix are myelosuppression, sensory neuropathy and neutropenia. Other minor side-effects include asthenia/fatigue, stomatitis, anorexia, alopecia, skin reaction, hypersensitivity reactions and a fluid-retention syndrome. Although Ix is functionally correlated to taxanes, no previous evidence exists regarding Ix-related nail disorders. On the contrary, taxanes can cause nail changes more commonly than other drugs (6, 7). Taxane-related nail abnormalities include nail pigmentation, splinter hemorrhage, subungual hematoma, Beau’s lines, acute paronychia and onycholysis. The occurrence of these disorders is more frequent after Docetaxel (D) than Paclitaxel (P) administration (6-9). Nail abnormalities occurring during taxane treatment are, in most cases, not severe, even though hemorrhagic onycholysis and subungual abscesses can produce important morbidity. Herein, we describe, for the first time, a case of nail disorders in a woman treated CT with Ix.

A 59-year-old patient, previously treated at our Institute for a left breast cancer (pT2 pN0 M0) with adjuvant chemotherapy (CT), including Epirubicin 120 mg/m² day 1 q 21 for 4 cycles and Cyclophosphamide 600 mg/m² Methotrexate 40 mg/m² Fluorouracil 600 mg/m² (CMF) days 1 and 8 q 28 for 4 cycles, was enrolled in October 2002 in an institutional phase II trial with Ix (40 mg/m² day 1 q 21 days) because of a lung relapse. She received 8 courses of therapy, achieving disease stabilization. After 6 cycles, the patient developed onycholysis and subungual hemorrhagic bullas in the fingernails (Figure 1). The treatment was not discontinued, and she received 2 additional courses of Ix. Although the dose of Ix was not reduced and a specific treatment started, we did not observe a worsening of the nail disorder. The cumulative

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Ix dose administered was 320 mg/m². Five months after ending of Ix infusion, the nail disorders were almost completely resolved.

Each physician must balance the potential benefits of novel treatments against potential adverse effects for their patients. In the case of our patient, the nail alteration was not so severe as to constitute a limitation for use of chemotherapy. However, this toxicity should not be underestimated, and patients pre-treated with taxanes or experiencing nail disorders after previous CTs should be controlled during and after treatment with Ix.

References


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