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An intermediate step for the management of hypersensitivity to platinum and taxane chemotherapy

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The guideline article "Management of hypersensitivity to platinum- and taxane-based chemotherapy: CEPO review and clinical recommendations" in this journal for the management of hypersensitivity reactions (HSR) to this group of chemotherapy agents is useful in clinical practice[1]. Administration of H_1 and H_2 blockers in addition to steroids and reduced infusion rates are important tools for a reactive oncology patient; they are also common intermediary steps for lesser hypersensitivity reactions before desensitization protocols are used[2]. Those approaches are effective in most, but not all, patients with taxane and platinum HSR.

During a taxane or platinum infusion–related HSR, antigen-stimulated mast cells release leukotrienes and prostaglandins in addition to histamine and other factors. Steroids (given preventively or as a therapeutic intervention) are thought to help reduce the production of leukotrienes and prostaglandins, among other actions. But we know from clinical practice that this intervention does not prevent all reactions. For patients in whom these usual approaches to managing HSR have failed, published reports have shown success with alternative therapies that block the pharmacologic effects of the prostaglandins and leukotrienes that are also released from mast cells that participate in the HSR[3,4].

Breslow *et al.*[5] reported that the use of montelukast and ASA, in addition to the above traditional means, have been successful in reducing both the severity and incidence of taxane and platinum HSR. Using an HSR grading system of 0 (absent), 1 (mild), 2 (moderate), and 3 (severe), he found a reduction in HSR severity from an average grade 2.14 to an average grade 0.5 when ASA and montelukast were used ($p < 0.001$). The biologic rationale is clear, given that montelukast blocks the leukotriene receptor and ASA blocks the effects of the prostaglandins, both offering additional and complementary means to avert the other mast-cell contributions to the HSR.

In our community cancer centre experience, of 375 taxane-, platinum-, and rituximab-based chemotherapy treatments given during a 6-week period (March and April 2014), 32 of the treatments resulted in HSR, prompting the use of montelukast alone or in combination with ASA, concomitant to the use of additional steroids, antihistamines, and H_2 blockers. Using the *Common Terminology Criteria for Adverse Events* system (version 4.0) to grade the severity of reactions [0, no reaction; 1, mild; 2, moderate; 3, severe (no epinephrine); 4, severe (epinephrine required); 5, death], we found that 45% had grade 3 reactions, followed by grade 2 (36%) and grade 1 (19%) reactions. Treatments in which montelukast with or without ASA was administered had significant amelioration of the HSRs, resulting in no inpatient admissions to hospital, no nursing overtime in the chemo suite, and no utilization of hypersensitivity dilution protocols for the patients. More importantly, no changes in the chemotherapy regimen protocols because of intolerance were observed, and subsequent treatments were delivered within the standard timeframes.

The use of additional agents is not without some potential risk to the patient, particularly in the case of ASA, and use of that drug must be weighed against possible benefit. A careful history, including bleeding risk and gastric medical history, should be considered. However, there can be substantial clinical benefit, especially in certain patient populations, such as those with diabetes, those sensitive to high-dose steroids, and those prone to restless leg syndrome as a result of diphenhydramine administration.

We suggest montelukast with or without ASA in HSR management as a possible effective means to avoid time-consuming—and sometimes ineffective—serial dilutions, and to maintain optimal therapeutic dosing and chair times. There is also an obvious cost–benefit to be achieved by using these relatively inexpensive agents to avoid prolonged chemotherapy chair time and reduce the use of nursing resources. There could be additional clinical scenarios in which a similar pharmacologic rationale exists and the use of these agents could be considered, such as cases of HSR to etoposide or rituximab—possibilities that warrant further exploration.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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