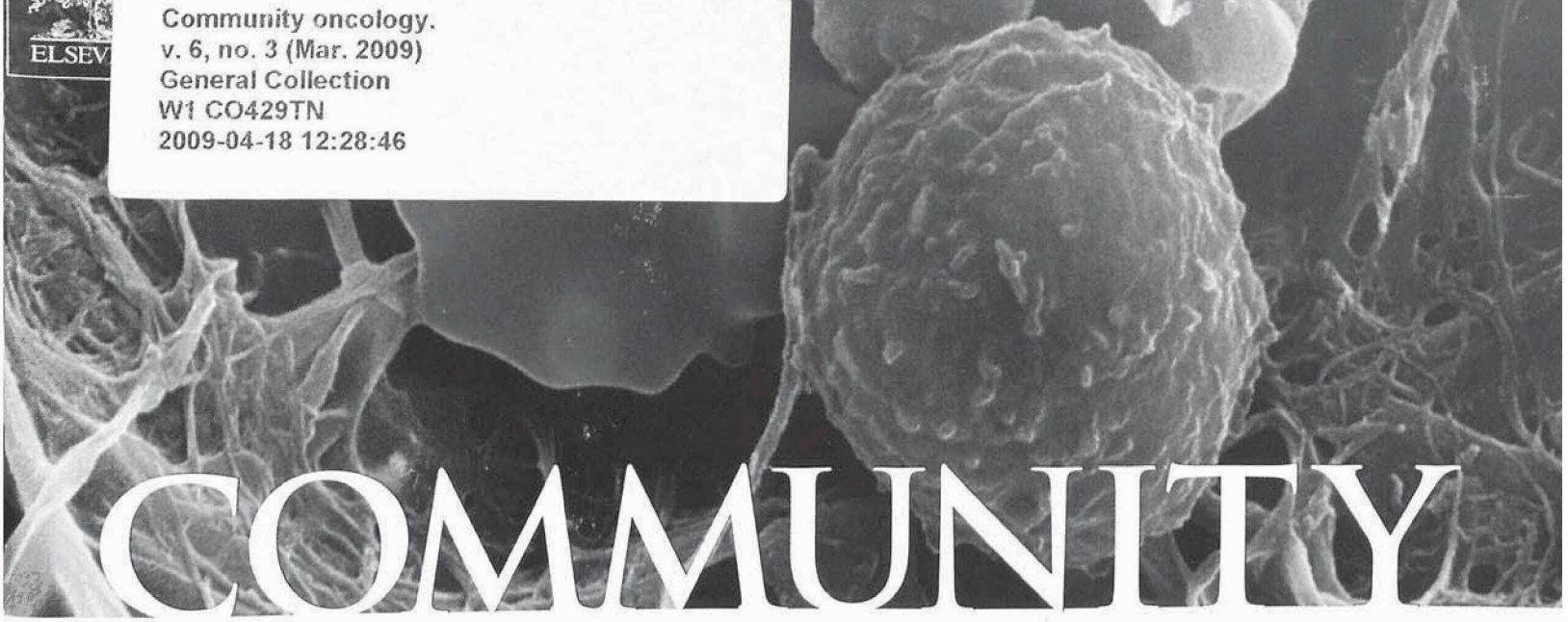

# COMMUNITY ONCOLOGY

THE ISSUES THAT MATTER TO YOU, YOUR PRACTICE, AND YOUR PATIENTS





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**On the cover** Colored scanning electron micrograph of blood cells in a patient suffering from leukemia. Four white blood cells (leukocytes, brown/green) and two red blood cells (erythrocytes, red) are seen. Photo: Steve Gschmeissner/Photo Researchers, Inc.

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# COMMUNITY ONCOLOGY

## Guide for Authors

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Editorial correspondence, including submissions for publication or Letters to the Editor, should be addressed to the Editor-in-Chief, Lee S. Schwartzberg, MD, FACP, e-mail: editor@communityoncology.net.

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BPA

# Cremophor EL-containing paclitaxel-induced anaphylaxis: a call to action

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Hypersensitivity reactions to Cremophor EL-containing paclitaxel range from mild pruritus to systemic anaphylaxis and can result in potentially severe clinical outcomes, including respiratory arrest, cardiac collapse, and death.[1]

## Fast Facts

ANAPHYLAXIS and severe hypersensitivity reactions are known to occur in patients during paclitaxel infusion. In early phase I studies of paclitaxel, there were a number of anaphylactic reactions and deaths, which raised great concern about the potential development of this drug.[2] Although the exact mechanism of these reactions to Cremophor-containing paclitaxel is not known, these responses are clinically consistent with a type I hypersensitivity reaction, an immediate, immunoglobulin E-mediated reaction. The hypersensitivity reactions may result from direct mast cell degranulation induced by either the chemotherapeutic agent itself or by Cremophor EL.[1,3]

It is generally believed that such reactions are due to the surfactant Cremophor EL, because these effects have also been observed in other drugs utilizing it. The amount of Cremophor EL used in paclitaxel is considerably larger than the amount used in other marketed products and anaphylaxis can occur despite the use of premedication.[2,4]

In Cremophor EL-containing paclitaxel clinical trials, up to 41% of patients experienced a hypersensitivity reaction. From 2%–4% of patients experienced anaphylaxis or a severe hypersensitivity reaction, characterized by dyspnea, hypotension, angioedema, and generalized urticaria.[5] Hypersensitivity reactions occurred even in patients who received prophylaxis.[6]

Up to 95% of hypersensitivity reactions to taxanes occurred during administration of the first or second dose, and almost 80% of symptoms developed during the first 10 minutes of infusion, with many reactions occurring after only 1 mg was infused.[1] A black-box warning on the drug's package insert alerts patients and healthcare professionals to the potential occurrence of fatal hypersensitivity reactions. Although hypersensitivity reaction prophylaxis is recommended, neither the frequency of use nor the efficacy of premedication prophylactic measures is known.

## Pharmacovigilance

As with all serious and potentially fatal adverse drug reactions, the US Food and Drug Administration (FDA) MedWatch database represents a valuable source of information. This is particularly relevant for Cremophor EL-containing paclitaxel-associated hypersensitivity, where the potential for severe anaphylaxis or death exists. No prior study has investigated FDA MedWatch reports for Cremophor EL-containing paclitaxel-associated hypersensitivity.

Investigators affiliated with the Research on Adverse Drug Events and Reports (RADAR), an established pharmacovigilance program, reviewed case reports of paclitaxel-induced hypersensitivity reactions from the FDA's Adverse Event Report System.[7] Our objectives were to 1) assess the quality and timing of individual case reports of serious or fatal paclitaxel hypersensitivity reactions submitted to regulatory agencies in the United States, Europe, and Japan; and 2) evaluate whether any of these events occurred despite the use of premedication prophylaxis (Table 1).

## What we reported

In a review of adverse event reports submitted to regulatory agencies between 1997 and 2007 in the United States, Europe, and Japan, 171 unique cases of Cremophor EL-containing paclitaxel-associated hypersensitiv-

*Dr. Raisch has an unrestricted grant from*

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