

# COMMUNITY ONCOLOGY

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

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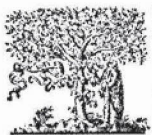
ADVERSE EVENTS ALERT

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Volume 6, Number 3, March 2009  
RUNNEMEDE NJ 08078-1161

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Community Oncology is  
published by



ELSEVIER

ONCOLOGY

Elsevier Oncology  
46 Green Street, 2nd Floor  
Huntington, NY 11743  
631.424.8900 tel • 631.424.8905 fax

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Community Oncology (ISSN 1548-5315) is published monthly by Elsevier Inc., Elsevier Oncology, 46 Green Street, 2nd Floor, Huntington, NY 11743. Periodicals postage paid at Huntington, NY, and additional mailing offices.

#### Change of Address

Postmaster: send address changes to *Community Oncology*, Circulation, Elsevier Inc., 60B Columbia Road, Morristown, NJ 07960.  
Recipient: to change your address, contact b.cavallaro@elsevier.com or mail to *Community Oncology*, Circulation, Elsevier Inc., 60B Columbia Road, Morristown, NJ 07960.

**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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### Guide for Authors

*Community Oncology* serves as a forum and resource for more than 31,000 practice-based oncologists, hematologists, oncology nurses, pharmacists, and administrators.

### TYPES OF ARTICLES

*Brief Communications* Short case reports.  
*Challenging Cases/Rare Cancers* Expert opinion and resources.

*Community Translations* places pivotal new research findings into the context of community practice.

*Controversies in Patient Management* looks at the difficult questions that arise when delivering quality care.

*Economics/Practice Management* How to make your practice more efficient.

*Having Your Say* Guest editorials.

*Managing Side Effects* Clinical articles on dealing with comorbidities.

*Nurse Management* Nursing perspective on patient care and managing side effects.

*Original Contributions* Peer-reviewed articles ranging from retrospective reviews to original observations and results of clinical trials conducted in the community setting.

*Practice Survival* Personal essays.

*Psychosocial Oncology* details the spiritual, psychological, social, and emotional side of cancer care.

*Quality Care* Issues ranging from pay-for-performance to implementing treatment guidelines in your practice.

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**The Editors require that authors disclose all potential conflicts of interest.**

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### LETTER FROM THE EDITOR

#### 99 **Cancer treatment: it's getting personal**

Lee S. Schwartzberg, MD, FACP, *The West Clinic, Memphis, TN*

This issue of *Community Oncology* focuses on a number of aspects of personalized medicine. At this moment, the grand vision of tailoring therapy to a tumor-specific target while calibrating dosages according to underlying subtle metabolic differences in each patient remains more a theory than a reality. Yet there has been remarkable progress already, with practical implications for clinicians.

### LETTER TO THE EDITOR

#### 105 **5-Fluorouracil-induced cardiotoxicity: hints for predicting patients at risk**

Jan Cerny, MD, and Bilal Piperdi, MD, *Department of Medicine, Division of Hematology and Oncology, University of Massachusetts Medical School, Worcester, MA*

**Dr. Tejwani responds**

Sheela Tejwani, MD, FACP, *Senior Staff Physician, Division of Hematology/Oncology, Josephine Ford Cancer Center, Henry Ford Hospital, Detroit, MI*

### BRIEF COMMUNICATIONS

#### 108 **Two patients with elevated alpha-fetoprotein levels and liver lesions in the absence of hepatocellular carcinoma**

Nazik Hammad, MD, MSc, Philip A. Philip, MD, PhD, and Bassel F. El-Rayes, MD, Hind Nassar, MD, and Kaleford Hong, MD, *Division of Hematology and Oncology, Karmanos Cancer Center, Wayne State University, Detroit, MI; Department of Pathology, Johns Hopkins University, Baltimore, MD; Department of Radiology, Wayne State University, Detroit, MI*

Two cases demonstrate the limitations of using alpha-fetoprotein levels to diagnose hepatocellular carcinoma in patients with hepatitis virus C infection.

### REVIEW ARTICLE

#### 113 **Identifying and treating imatinib failure in chronic myelogenous leukemia: a practical review of treatment guidelines and available agents**

Stuart L. Goldberg, MD, and Aisha Masood, MD, *Division of Leukemia, The John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ*

Although most patients respond to imatinib and achieve prolonged remission, the development of imatinib resistance has emerged as a major clinical issue. Two recently approved tyrosine kinase inhibitors, the dual BCR-ABL and SRC inhibitor dasatinib and the imatinib analogue nilotinib, have shown substantial activity among patients with resistance or intolerance to imatinib. Given these new options, identification of nonresponders has become increasingly important to ensure the earliest administration of appropriate therapy. The authors review recommendations for identifying and treating patients with chronic-phase chronic myelogenous leukemia who have experienced failure of first-line imatinib.



# COMMUNITY ONCOLOGY

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## PHARMACOGENETICS

### 126 Personalized therapy for cancer: has pharmacogenetics delivered?

Jeffrey Allen, MD, and Clinton F. Stewart, PharmD, *University of Tennessee Cancer Institute, Memphis, TN, Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, TN*

The prescribing information for several drugs has already been changed on the basis of pharmacogenetic data. In addition, two drugs—irinotecan, a camptothecin analog with activity in a number of solid tumors, and tamoxifen, a selective estrogen receptor modulator with activity in breast and uterine cancers—have been the focus of intense pharmacogenetic investigations over the past decade. For patients and oncologists alike, pharmacogenetic studies on these drugs and others are opening the door to a new era of personalized anticancer therapy.

## ADVERSE EVENTS ALERT

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

Lauren D. Irizarry, BA, Thanh Ha Luu, BA, June M. McKoy, MD, JD, MPH, Athena T. Samaras, BA, Matthew J. Fisher, BA, Edson E. Carias, BA, Dennis W. Raisch, PhD, RPh, Elizabeth A. Calhoun, PhD, and Charles L. Bennett, MD, PhD, MPP, *Division of Hematology/Oncology, Northwestern University, Feinberg School of Medicine, Chicago, IL; VA Midwest Center for Management of Complex Chronic Care, Jesse Brown VA Medical Center, Chicago, IL; Division of Geriatric Medicine, Northwestern University, Feinberg School of Medicine; The Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL; University of New Mexico College of Pharmacy and VA Cooperative Studies Program, Albuquerque, NM; University of Illinois, Chicago, IL*

Published literature indicates that hypersensitivity reactions to cremophor-containing paclitaxel occur quite often and are of varied severity. The authors review the problem and make a number of recommendations for prevention and treatment.

## WASHINGTON UPDATE

### 135 The tallest order: fixing the economy and healthcare

Caroline Helwick

The current fiscal crisis is taking center stage, and although healthcare is a key part of our financial woes, fixing the economy will have to come first—at least for now. A report on the legislative roundtable at the 4<sup>th</sup> Annual Community Oncology Conference.



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

Lauren D. Irizarry, BA,<sup>1,2</sup> Thanh Ha Luu, BA,<sup>1,2</sup> June M. McKoy, MD, JD, MPH,<sup>3,4</sup> Athena T. Samaras, BA,<sup>1,2</sup> Matthew J. Fisher, BA,<sup>1,2</sup> Edson E. Carias, BA,<sup>1,2</sup> Dennis W. Raisch, PhD, RPh,<sup>5</sup> Elizabeth A Calhoun, PhD,<sup>6</sup> and Charles L. Bennett, MD, PhD, MPP<sup>1,2,4</sup>

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**H**ypersensitivity 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.<sup>1</sup>

## 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.<sup>2</sup> 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.<sup>1,3</sup>

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.<sup>2,4</sup>

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.<sup>5</sup> Hypersensitivity reactions occurred even in patients who received prophylaxis.<sup>6</sup>

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.<sup>1</sup> 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 repre-

sents 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.<sup>7</sup> 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 hypersensitivity

*Dr. Raisch has an unrestricted grant from*

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