

12-2006

OncoLog Volume 51, Number 12, December 2006

Sunni Hosemann

The University of Texas MD Anderson Cancer Center

Follow this and additional works at: <https://openworks.mdanderson.org/oncolog>

 Part of the [History of Science, Technology, and Medicine Commons](#), and the [Oncology Commons](#)

Recommended Citation

Hosemann, Sunni, "OncoLog Volume 51, Number 12, December 2006" (2006). *OncoLog MD Anderson's Report to Physicians (All issues)*. 190.

<https://openworks.mdanderson.org/oncolog/190>

This Newsletter is brought to you for free and open access by the OncoLog MD Anderson's Report to Physicians at OpenWorks @ MD Anderson. It has been accepted for inclusion in OncoLog MD Anderson's Report to Physicians (All issues) by an authorized administrator of OpenWorks @ MD Anderson. For more information, please contact rml-help@mdanderson.org.

A Publication of
**M. D. Anderson
 Cancer Center**
Making Cancer History®

3
**Hodgkin's
 Lymphoma Protocols**
 A list of open
 clinical trials

4
In Brief
 Novel agent prevents
 bone tumors, and
 more

5
House Call
 Big benefits
 for smokers
 who quit



6
**Updating Our
 Mailing List**
 How to continue
 receiving *OncoLog*

REPORT TO PHYSICIANS

DECEMBER 2006 Vol. 51, No. 12

OncoLog

Curable But Not Conquered: Hodgkin's Lymphoma Today

Reducing long-term toxicity is an
 important focus of clinical trials

by **Sunni Hosemann**

The impact of cancer is often brought home to us by numbers: how many people it strikes, how many will die from it, and how short or long will be the time between. Hodgkin's lymphoma is not the most prevalent or the most deadly type of cancer. The coming year will see perhaps 7,800 new cases in the United States, and of those, more than 80% will be cured.

To appreciate the real impact of Hodgkin's lymphoma, one must view it in terms of productive life years either lost altogether or marked by lingering morbidity, explained Anas Younes, M.D., professor of medicine and director of Clinical and Translational Research at The University of Texas M. D. Anderson Cancer Center's Department of Lymphoma. The main target of Hodgkin's lymphoma is the young: for a 20-something patient who dies of the disease, perhaps a half-century of productive years are lost; those cured remain at increased risk for related illnesses or long-term complications that will potentially shorten their lives.

Although in the field of oncology, an 80% cure rate is an unqualified success, Dr. Younes thinks it
(Continued on next page)



Developing treatments with fewer complications is a key focus for
Dr. Michelle Fanale (l) and
Dr. Anas Younes (r).

THE UNIVERSITY OF TEXAS
**MD ANDERSON
 CANCER CENTER**

Hodgkin's Lymphoma Today

(Continued from page 1)

would be short-sighted to assume that because there is a *good* standard treatment, there is no need to continue searching for something *better*.

Finding something better is the focus of Dr. Younes and his colleague Michelle Fanale, M.D., an assistant professor in the Department of Lymphoma, who together oversee clinical trials for Hodgkin's lymphoma at M. D. Anderson. They want "cure" to mean more than freedom from Hodgkin's. They want it to mean a long, healthy life.

Where we are today

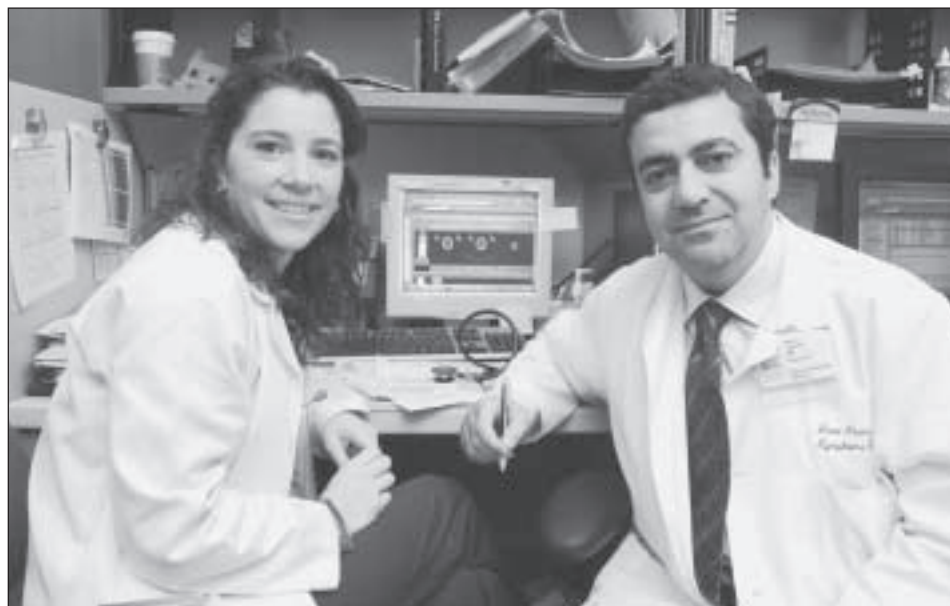
Hodgkin's lymphoma has been considered curable in most patients for over three decades, with the use of various combinations of chemotherapy and radiation. The current standard treatment for early-stage disease is combination chemotherapy ABVD (Adriamycin, bleomycin, vincristine, and dacarbazine) with or without radiation therapy. More potent (and therefore more grueling) treatments are used in advanced, refractory, or recurrent disease, including more powerful drugs and drug combinations and high-dose regimens with bone marrow or stem cell transplants.

Despite the high cure rate, many of these patients—many of whom are in the prime of their lives—will experience long-term effects related to these treatments: they may develop leukemias, non-Hodgkin's lymphomas, sarcomas, melanomas, cancers of the breast, thyroid, and lung, or cardiac and pulmonary diseases. The high cure rate of Hodgkin's lymphoma and the relatively young age of most patients makes complications more likely to arise in their lifetimes.

Paralleling general trends in oncology, the quest for better treatments for this disease is focused on two goals: to improve efficacy and to reduce side effects and long-term morbidities. In medical oncology today, those goals are pinned on new molecular agents that can more specifically target tumor cells without harming healthy ones.

Novel therapies

According to Dr. Younes, there are two fundamental targets for new agents



Amanda Wedgwood (l) and Dr. Anas Younes (r) are seeking more patients for clinical trials of Hodgkin's lymphoma treatments.

in clinical trials for Hodgkin's lymphoma: the well-known Reed-Sternberg (RS) tumor cells that are the hallmark of this disease and the benign reactive cells that surround them (B and T cells, monocytes, and eosinophils).

"These cells have been shown to be contributors, rather than the benign bystanders they were once thought to be," said Dr. Fanale. "They support the survival and growth of the tumor cells by providing key cell signaling processes." In fact, researchers have found that tumor cells are difficult to culture in their absence. Dr. Younes noted the irony of host immune cells providing survival factors to malignant cells, a sort of "immune betrayal." But now that their role has been clarified, he said, "The use of novel agents to eliminate these reactive cells from the microenvironment may deprive the tumor cells of critical survival factors, causing their death." Most of the novel agents are either monoclonal antibodies or small molecules.

Monoclonal antibodies are engineered to bind to a specific protein on a cell surface, causing an immune

response to those cells. For specificity, the key is to find a protein that is unique to—or expressed in abundance by—the target cells. Rituximab is an example of a drug that targets the CD20 protein that has been used successfully in non-Hodgkin's lymphomas and, more recently, by Dr. Younes for Hodgkin's lymphoma. This was considered a novel use: because CD20 is not frequently expressed by the RS tumor cells in Hodgkin's lymphoma, it hadn't been formally investigated for that disease. But the B cells in the microenvironment do express CD20, and Dr. Younes got



Dr. Michelle Fanale (l) and Mona Gilliam (r) discuss treatment plans for a young patient with Hodgkin's lymphoma.

encouraging results from an ongoing clinical trial combining anti-CD20 antibody (rituximab) with ABVD chemotherapy.

Anti-CD30 agents, on the other hand, are targeted to the RS cells themselves, where CD30 is abundantly expressed. According to Dr. Fanale, when given as a single agent in a recent phase I-II clinical trial, anti-CD30 produced remissions in some patients. “Now we’re building on that,” she said. “In a new trial, for example, we will use an anti-CD30 antibody in combination with gemcitabine chemotherapy in combination with a dexamethasone, and we will compare these results with gemcitabine chemotherapy alone.”

Small molecules are agents that act by disrupting signaling pathways critical to the life of the cell, often by interfering with receptors or regulatory enzymes such as histone deacetylase (HDAC) used by the cell to maintain its biologic life functions. One of the current phase II studies uses an HDAC inhibitor for patients with relapsed Hodgkin’s lymphoma. 17-AAG (17-allylamino-17-demethoxy-geldanamycin) is another small molecule that affects cell proliferation and cell death functions. Furthermore, other agents such as AMG-531, a thrombopoietin-like agent, are being evaluated to potentially decrease the incidence of thrombocytopenia during chemotherapy.

Current trials: the patient experience

The advantages of new agents are that they have fewer side effects, and some of them can be taken orally. According to Amanda Wedgwood, an advanced practice nurse who coordinates the Hodgkin’s lymphoma trials, the oral formulation and ease of protocols is a source of relief and even delight for patients accustomed to the more grueling standard treatments.

In one current study, patients with relapsed disease take an oral HDAC inhibitor three times a week and come to M. D. Anderson for checkups once a month. “The fact that they can do this at home and still see their own physicians is important to our patients,

especially since most of them don’t live in Houston,” said Ms. Wedgwood, who nevertheless keeps in touch with her patients and encourages them and their physicians to contact her with any questions or concerns.

“Staying in contact is an important factor,” she said. “It just makes people feel secure. But the best part of this trial is how easy and gentle these treatments are compared with what many of them have been through before.” The side effects are minimal—fatigue is the major one.

Drs. Younes and Fanale, along with Ms. Wedgwood, are buoyed by the success they have seen so far and optimistic that it may lead to new standard treatments. For that to happen, though, they need more patients in trials. “Things are moving in Hodgkin’s lymphoma research—moving fast,”

said Dr. Younes. “But not fast enough. Enrollment numbers in our trials are lower than we’d like. We want to change that by getting the word out that we can achieve not just better short-term survival and remission rates, but also hopefully have a long-term impact in the form of longer remission and lower toxicity rates.”

Clinical trials are available for patients of all ages with any stage of Hodgkin’s lymphoma, including those newly diagnosed who have had no previous treatment, those in first relapse, and those who have had extensive treatment. For more information, visit www.mdanderson.org/departments/lymphmyeloma. ●

FOR MORE INFORMATION, contact Dr. Younes or Dr. Fanale at (713) 792-2860.

HODGKIN’S LYMPHOMA PROTOCOLS

- Phase II study of rituximab + ABVD for patients with Hodgkin’s lymphoma (ID00-218). Physician: Anas Younes, M.D.
 - Phase II study of 17-AAG in patients with relapsed/refractory CD30-positive anaplastic large cell lymphoma, relapsed/refractory mantle cell lymphoma, or relapsed/refractory classical Hodgkin’s lymphoma (2004-0792). Physician: Anas Younes, M.D.
 - Open-label dose and schedule-finding trial to evaluate the safety and efficacy of AMG 531 for treatment of severe thrombocytopenia due to multicycle chemotherapy in adult subjects with relapsed aggressive lymphoma (2005-0749). Physician: Michelle A. Fanale, M.D.
 - Phase I/II, non-randomized, multiple-dose, dose-escalation study of the safety, pharmacokinetics, pharmacodynamics, and efficacy of TNX-650 in patients with refractory Hodgkin’s lymphoma (2006-0011). Physician: Anas Younes, M.D.
 - Multicenter, open-label, phase II study of single-agent GX15-070MS administered as a 24-hour infusion every 2 weeks to patients with relapsed/refractory Hodgkin’s lymphoma (2006-0441). Physician: Anas Younes, M.D.
 - Phase II study of MGCD0103 (MG-0103) in patients with relapsed/refractory Hodgkin’s lymphoma (2006-0465). Physician: Anas Younes, M.D.
 - Phase I dose-escalation study of SGN-35 in patients with relapsed/refractory CD30-positive hematologic malignancies (2006-0475). Physician: Anas Younes, M.D.
 - Open-label, randomized, multicenter, phase II study of MDX-060 (humanized anti-CD30 antibody) in combination with gemcitabine, MDX-060 in combination with dexamethasone, and gemcitabine monotherapy in relapsed/refractory Hodgkin’s lymphoma (2006-0027). Physician: Michelle A. Fanale, M.D.
- FOR MORE INFORMATION** and a broader listing of trials, visit www.clinicaltrials.org or call askMDAnderson at 1-877-MDA-6789. ●

New Agent May Thwart Bone Metastasis

A novel agent targeting the vascular system completely prevented the development of bone tumors in 50% of the mice tested in a preclinical study, providing early evidence that the agent could treat, or thwart, the growth of tumors in the bone, a common site of metastasis for a number of cancers.

Researchers at M. D. Anderson Cancer Center reported in the November 15 issue of the journal *Cancer Research* that this agent, VEGF121/rGel, stopped specialized cells within the bone from destroying other bone material; otherwise, the destruction makes room for the implanted tumor to grow.

Although this study specifically tested the ability of VEGF121/rGel to halt the growth of human prostate cancer cells in the bones of mice, investigators say it likely could help prevent other cancers, such as breast cancer, multiple myeloma, lung cancer, and renal cell carcinoma, from metastasizing to bones as well.

“Many tumors invade bone in the same way, so these findings suggest it may be possible to shut down this process regardless of the tumor type,” said the study’s lead author, Michael G. Rosenblum, Ph.D., professor in the Department of Experimental Therapeutics. “We’re a long way from determining if it’s possible in humans and in all tumor types; phase I clinical trials are expected to open shortly at M. D. Anderson to explore this. But if we find it can be done, it could lead to the first treatment that specifically targets bone metastasis.”

The study also revealed critical information about the role of vascular endothelial growth factor (VEGF) in the development of tumors in bone, said Dr. Rosenblum. VEGF is a signaling protein involved in the creation of new blood vessels, but the researchers found that it plays a surprising role in the remodeling of bone tissue as well.

Because tumor cells that metastasize to bone release VEGF, the researchers did not know whether the protein

interrupted bone maintenance or promoted the growth of blood vessels to feed the neophyte cancer, Dr. Rosenblum said.

To find out, Dr. Rosenblum designed an experiment with VEGF121/rGel, an agent designed to enter new blood vessel cells in tumors through expressed VEGF receptors. Once inside, the “Trojan horse” toxin destroys the cell, disrupting the ability of tumors to form the vascular systems necessary for growth. Previous laboratory studies have shown that the protein can selectively destroy blood vessels feeding human solid tumors.

VEGF121/rGel stops the bone destruction needed for the cancer to grow and may also inhibit blood vessel growth to the metastasized tumor.

Half of the treated mice did not develop any bone tumors, Dr. Rosenblum said. “We don’t know why the treatment worked in half of the mice and not the others (the cells of which were genetically identical), but we may have started therapy too late in those that didn’t respond,” he said.

Researchers determined that VEGF121/rGel may work through two different VEGF receptors. It stops the bone destruction needed for the cancer to grow and may also inhibit blood vessel growth to the metastasized tumor, Dr. Rosenblum said.

“The fact that this form of VEGF targeting works on different cell receptors in blood vessels and in bone cells is a unique finding that could be clinically significant, not only in treating cancer but also in other bone disorders,” he said. “At the very least, this study gives us a better understanding of how VEGF operates and how it is involved in bone remodeling.”

Innovative AML Treatment Proves Promising

Acute myeloid leukemia (AML) is known for its resistance to standard chemotherapy treatment. Now, researchers at M. D. Anderson Cancer Center have found, in laboratory studies, that the experimental drug ABT-737 can destroy AML blast, progenitor, and even stem cells.

The drug was potent in its own right, the researchers said, but they found that some types of AML cells were resistant to ABT-737, so they added another drug, a MAP-kinase inhibitor, that overcame this resistance. Together, these agents hold promise as a new therapy for AML and could eventually form the basis of a new way to treat the cancer, said the scientists, whose study was published in the November 14 issue of the journal *Cancer Cell*.

“The combination of these two experimental drugs provides the highest synergistic action I have ever seen against acute myeloid leukemia cells,” said the study’s lead author, Michael Andreeff, M.D., Ph.D., professor in the Departments of Stem Cell Transplantation and Leukemia. “ABT-737 would overcome resistance to chemotherapy that we often see in AML therapy, and the MAP-kinase inhibitor would overcome resistance to ABT-737,” he said.

ABT-737 targets the best-known member of the BCL-2 family of proteins, also called BCL-2, which prevents a cell from undergoing apoptosis. ABT-737, however, was engineered to fit tightly on BCL-2, occupying the BCL-2 binding space so that other proteins can promote apoptosis.

In this study, Dr. Andreeff and a team of researchers found that ABT-737 “potently” kills AML cell lines as well as blast cells taken from AML patients. “Most importantly, our results demonstrated destruction of the progenitor and stem cells responsible for production of AML, which makes this a truly innovative treatment with potential application in different leukemias and solid tumors,” Dr. Andreeff said.



Big Benefits for Smokers Who Quit

Everyone knows that smoking is bad for your health, but the stark facts may still be surprising:

- Tobacco use is the single most preventable cause of death in the United States, responsible for nearly one in five deaths in 2006 alone.
- The number of yearly deaths from smoking is far greater than those from all accidents, suicides, drug use, homicides, and AIDS combined.
- An estimated 45 million adults in this country are smokers, and more than one third of U.S. high school students smoke.

Tobacco and cancer

Tobacco causes 87% of lung cancer deaths and 30% of all cancer deaths, according to the American Cancer Society. Tobacco use in any form—cigarettes, chewing tobacco, pipes, and cigars—also increases the risk for developing cancers of the head and neck, esophagus, stomach, liver, pancreas, kidney, bladder, uterus, cervix, and colon and rectum, as well as heart disease, stroke, and a variety of lung diseases.

Not only does tobacco affect the health of smokers, it also harms those around them. The U.S. Surgeon General this year issued a report detailing the health effects of involuntary exposure to tobacco smoke, concluding that secondhand smoke causes premature death and disease in children and adults who do not smoke. Children exposed to secondhand smoke have an increased risk of developing a variety of health problems: acute respiratory infections, asthma, ear infections, and even sudden infant death syndrome. New research suggests that secondhand smoke also is harmful to children's brains.

Quitting tobacco

But, as many smokers know, quitting isn't easy. The nicotine in tobacco is extremely addictive, quickly causing physical and psychological dependency. Yet quitting is possible, and recent research in smoking cessation is finding ways to make it easier.

So what's the best way to quit?

Research shows that quitting smoking is best accomplished under the guidance of experts, according to Paul Cinciripini, Ph.D., professor and deputy chair of M. D. Anderson Cancer Center's Department of Behavioral Science. "Tobacco cessation is no longer a one-size-fits-all approach," he said. "At M. D. Anderson, we have a variety of stop-smoking programs targeted at specific groups such as pregnant women, cancer patients, new mothers, and teenagers."

Methods that have proven especially successful include nicotine replacement therapy, medications, counseling, and support groups. Nicotine substitutes, such as the nicotine gum and patches available over the counter at many drugstores, gradually reduce the smoker's nicotine levels. Prescription antidepressants, such as bupropion (Wellbutrin), reduce withdrawal symptoms, while a new nicotine-blocking drug, varenicline (Chantix), partially activates nicotine receptors in the brain to reduce the severity of cravings.

Changing the smoking habit

Changing habits and behaviors associated with smoking also can be helpful. This might mean

- avoiding other smokers or asking them not to smoke around you.
- cutting back on alcohol, coffee, or other beverages you associate with smoking.



The Good News:

Smokers who quit before the age of 50 cut in half their risk of dying within the next 15 years.

After 10 to 15 years of not smoking, the risk of premature death is close to that of a non-smoker's.

- getting rid of tobacco and ashtrays at home, work, and in your car.
- learning how to handle stress by practicing relaxation techniques.
- making a list of situations that make you want to smoke and then coming up with some substitute activities to do the next time you're tempted.

Benefits of quitting

The benefits of quitting are huge. Research has shown that significant health benefits occur almost immediately, even for long-term smokers. Smokers who quit before the age of 50 cut in half their risk of dying within the next 15 years. After 10 to 15 years of not smoking, the risk of premature death is close to that of a non-smoker's.

MORE INFORMATION about tobacco and cancer is available online at www.mdanderson.org/topics/smoking.

For more information, talk to your physician, or:

- call askMDAnderson at (877) MDA-6789
- visit www.mdanderson.org.

December 2006

K. Stuyck

©2006 The University of Texas
M. D. Anderson Cancer Center

OncoLog

The University of Texas
M. D. Anderson Cancer Center
Department of Scientific Publications-234
1515 Holcombe Boulevard
Houston, Texas 77030-4009

www2.mdanderson.org/depts/oncolog

Address Service Requested

Nonprofit Org.
U.S. Postage
PAID
Permit No. 7052
Houston, TX

We Don't Want to Lose You! *So please save this page.*

OncoLog's mailing list will undergo some changes in the next few months, and it's possible some addresses will be inadvertently omitted in the conversion. Most physicians should continue to receive *OncoLog* uninterrupted, but should you miss an issue of *OncoLog* (or if you want to contact us now to ensure that your name stays on the list), you can do that in several ways.

To subscribe to the online version:

Go to the *OncoLog* Web site at www2.mdanderson.org/depts/oncolog. Click "Sign Up for E-mail Alerts" to receive notification when an issue is posted.

To subscribe to the print version:

Go to the *OncoLog* Web site at www2.mdanderson.org/depts/oncolog. Click "Contact *OncoLog*" to request that we keep your name on the mailing list.

You can also contact us by:

Phone (713) 792-3305
Fax (713) 794-1370
E-mail scientificpublications@mdanderson.org
(Subject: OncoLog Mailing List)
U.S. mail *OncoLog* Mailing List
Department of Scientific Publications – Unit 234
M. D. Anderson Cancer Center
1515 Holcombe Blvd.
Houston, TX 77030

To ensure
that your issues
of *OncoLog*
keep coming,
contact us
today!

In any correspondence, please include your name, the name of your practice and/or specialty, your business address, phone, and e-mail address.

OncoLog

The University of Texas
M. D. Anderson Cancer Center

President
John Mendelsohn, M.D.

**Executive Vice President
and Chief Academic Officer**
Margaret L. Kripke, Ph.D.

Senior Vice President for Academic Affairs
Stephen P. Tomasovic, Ph.D.

**Director, Department of
Scientific Publications**
Walter J. Pagel

Managing Editor
Dianne C. Witter

Assistant Managing Editor
Martha Morrison

Contributing Editors
Dawn Chalaire
Manny Gonzales
Sunni Hosemann
Angelique Siy
Karen Stuyck

Design
The Very Idea®

Photography
Jim Lemoine

Editorial Board
Michael Fisch, M.D., *Chair*
Lyle Green, *Vice Chair*
Therese Bevers, M.D.
Elihu Estey, M.D.
Robert Gagel, M.D.
Beverly Handy, M.D.
Patrick Hwu, M.D.
Maurie Markman, M.D.
Shreyaskumar Patel, M.D.
David Schwartz, M.D.
Rena Sellin, M.D.
Randal Weber, M.D.
Christopher Wood, M.D.

OncoLog, M. D. Anderson Cancer Center's report to physicians, is a monthly newsletter sent to more than 30,000 physicians throughout the nation and the world. Published by the Department of Scientific Publications, *OncoLog* reports on innovative developments in research and treatment at M. D. Anderson. Current and previous issues are available online in English and Spanish at www2.mdanderson.org/depts/oncolog. For editorial information, call (713) 792-3305 or email scientificpublications@mdanderson.org. To refer a patient or request information, call (800) 392-1611 or (713) 792-6161, or visit www.mdanderson.org.

Made possible in part by a gift from the late Mrs. Harry C. Wiess.

NCI® A Comprehensive Cancer
CCC Center Designated by the
National Cancer Institute