SCRIPTDOCTOR: MEDICINE IN THE MEDIA

How an *ER* Storyline Helped Pass the Patient Navigator Act

By Andrew Holtz, MPH

Andrew Holtz, MPH, is a former CNN Medical Correspondent and the author of "The Medical Science of House, M.D." This column examines mass media programs, particularly entertainment TV, for insight into popular perceptions, so that rather than merely wincing at distortions or oversimplifications in the portrayals of medicine on these shows, health care professionals can learn something from media professionals about the way that medical and health topics are presented. ***Send questions to him about how the media treat medical topics or suggestions for future columns to OT@lwwny.com***

It's a happy picture: President Bush beaming, flanked by smiling members of Congress, as he signs the Patient Navigator Outreach and Chronic Disease Prevention Act of 2005. It was one of the few pieces of health care-related pieces of legislation to reach his desk during the last session.

"For a bill that, in the scheme of things, was small, for it to rise to the level where the President invites the members of Congress who were involved in this effort to the White House and they have a signing ceremony in the Oval Office, with photographs and such; that's pretty amazing," says Licy DoCanto, who was with the American Cancer Society's Government Relations Office at the time.

For reasons I'll explain shortly, I took a personal interest in the recollections of DoCanto and other supporters of patient navigator programs, such as former Harlem Hospital Cancer Chief Harold Freeman, MD. They have pushed for many years to expand the use of these trained lay people, who help guide patients through treatment and bridge the gulf between the worlds of patients and physicians. They used all the standard lobbying techniques to move a bill funding more patient navigator programs.

But they also got an assist from some unusual "testimony:"

> *In the ER hallway, Dr. Ray Barnett and Dr. Gregory Pratt look back at a cancer patient and another woman talking inside Trauma Room One.*
>
> *Barnett: "Where'd you find her?"*
>
> *Pratt: "There's a cancer support group upstairs. They have patient navigators to help people get through the system."*

Clips of an episode of *ER* featuring a patient navigator were played for legislators and key staffers in what could be thought of as a twist on the tried-and-true technique of bringing a Hollywood celebrity to Washington to open doors and perhaps win some votes.

'Refusal of Care' Episode

In the episode titled "Refusal of Care," doctors were trying to persuade a reluctant patient to accept treatment for the advanced cancer they had stumbled on while treating her for a bone fracture. The woman blocked out the pleas of white-coated physicians, but opened up to a cancer survivor.

"I brought it to them," says DoCanto. "Here we took a very popular program and we said, 'Even *ER* has picked up on the importance of patient navigation and if even they have, then you've got to know that there's relevance for this. So it was another way of stimulating the people who were working on it."

DoCanto notes that members of Congress are besieged by pleas for action…so anything that can cut through the clutter is useful. "They are real people, too. They watch these programs. I think they do have an impact."

DoCanto got the video from Dr. Freeman, who had worked with *ER* writers to create the storyline.

Dr. Freeman, now a Senior Adviser to the Director of the NCI on cancer disparities and Medical Director of the Ralph Lauren Center for Cancer Care and Prevention in New York City, says the collaboration began with a briefing set up by the Hollywood, Health & Society program at USC Annenberg's Norman Lear Center. He told the *ER* writers about patients who resisted surgery because they had the mistaken belief that if air touches a tumor, the cancer will spread.

> *"Members of Congress are besieged by pleas for action, so anything that can cut through the clutter is useful. They are real people, too. They watch these programs. They do have an impact."*

Dr. Freeman, a member of *OT*'s Editorial Board, said he suspects the myth may spring from stories of people who did not appear to be seriously ill until after they were treated.

"The community translates the case into, I believe: 'John walked into the emergency room. He was strong enough to walk in. They operated on him. He seemed to tolerate the surgery okay; he was discharged in 10 days. And then he died.' So the translation is: 'The air touched the cancer and caused the cancer to spread,'" Dr. Freeman said.

The pervasiveness of this belief was documented in a 2003 survey by Mitchell L. Margolis, MD, and colleagues at the Philadelphia VA Medical

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Osseous-Epithelial

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prostate cancer progression and may account for how prostate cancer presents in the clinic, he said. The clinical implication is that those pathways become further targets to consider in inhibiting the disease.

Combination Key

As with many other newly developed targeted therapies, treatments targeting the stromal-epithelial connection would have to be used as part of a combination regimen, Dr. Logothetis said. Blocking the bone stroma alone would not be curative, although it could be a strategy to prolong survival.

"Therapies blocking the stroma plus cytotoxic therapies is how we envision it," he said.

Early Clinical Research with Thalidomide

He described early clinical research at M. D. Anderson using thalidomide, an agent that is active in disrupting the interaction between a primary prostate cancer tumor and the bone stroma. Thalidomide is not an ideal drug for this purpose because of its adverse effects, he noted, but there are new agents in development that do possess many of the properties of thalidomide without the toxicity.

Dr. Logothetis said researchers saw a disruption of the stromal-epithelial interaction with thalidomide administration, but importantly this was seen prior to any evidence of an effect on the epithelial compartments.

This validated the principle of targeting the host component in metastatic disease as a therapeutic approach.

He mentioned some of the new agents in ongoing experiments that might interfere with this interaction: Atrasentan, a selective endothelin-A receptor antagonist, was the first to enter major trials and is now being tested in combination with chemotherapy. Sunitinib, an inhibitor targeting several receptor tyrosine kinases, is also being studied in combination with chemotherapy, as is the Src oncogene inhibitor dasatinib. And researchers will soon be using insulin-like growth factor-1 blocking pathways in combination with chemotherapy, he said.

'Cutting Edge'

Another speaker at the meeting, Gregory R. Mundy, MD, the John A. Oates Chair in Translational Medicine and Director of the Vanderbilt University Center for Bone Biology, spoke about this osseous-epithelial interaction in an interview at the meeting.

"That's just been characterized in the last several years, and it's clearly going to be very important for metastasis and maybe for the dormant state of some tumor cells," Dr. Mundy said. "That's cutting-edge stuff."

He said other speakers had described how cells now being identified in the bone marrow actually prepare the metastatic site of the tumor cells to later settle down and grow. These are also in the bone marrow, he said, but presumably the whole process is directed by the primary tumor cells.

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Center and University of Pennsylvania, the Los Angeles VA Medical Center, and the Medical University of South Carolina. Of 626 consecutive patients in pulmonary and lung cancer clinics, 38% stated that they believe air exposure at surgery causes tumor spread. The belief was more common among African-American patients, with almost one in five saying it was a reason for opposing surgery.

"So I said," Dr. Freeman recalled, "'Maybe you should create a scene in which you have a patient who believes that. And then I said, 'Hopefully, you could utilize something I developed, and that is a patient navigator, who is a lay person who can talk to people, and those people will tend more to listen to somebody who looks and talks like them.' They then created an episode that involves both of those things."

ER writer Joe Sachs, MD, picks up what happened next: "So we did a story where [the character of Dr.] Pratt confronted, but couldn't get through to, this woman who absolutely refused surgery."

Scene in Trauma One as Dr. Pratt and Dr. Barnett examine cancer patient Debra Graham:

Graham: "You want to cut me? I don't think so.
Dr. Pratt: "An operation may be part of the treatment plan."
Agitated, Graham sits up, tries to get out of bed.
Graham: "Where are my clothes?"
Dr. Barnett: "Take it easy, you're all hooked up."
Alarms sound as some of the monitor cables disconnect.
Graham: "I never should have come here."
Dr. Pratt: "You need to stay."
Graham: "I don't want you cutting into me."
Pratt and Barnett have to hold her down for her own safety.
Dr. Pratt: "Relax."
Graham: "No, no…"
Dr. Barnett: "It's okay…"
Graham: "You don't cut into cancer…"
Dr. Barnett: "We're not going to."
Graham: "I know what happens."
Dr. Pratt: "Settle down."
Graham: "You cut into cancer, it spreads…"
Dr. Pratt: "Mrs. Graham…"
Graham: "It spreads and you die."

Dr. Sachs says he was drawn to the topic because it allowed them to explore Dr. Pratt's struggle with the gap that had developed between him and the world he had grown up in. He

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however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

Immunogenicity
As with all therapeutic proteins, there is potential for immunogenicity. Potential immunogenic responses to Cetuximab were assessed using either a double antigen radiometric assay or an enzyme-linked immunosorbant assay. Due to limitations in assay performance and sampling timing, the incidence of antibody development in patients receiving ERBITUX (Cetuximab) has not been adequately determined. The incidence of antibodies to Cetuximab was measured by collecting and analyzing serum pre-study, prior to selected infusions and during treatment follow-up. Patients were considered evaluable if they had a negative pre-treatment sample and a post-treatment sample. Non-neutralizing anti-Cetuximab antibodies were detected in 5% (49 of 1001) of evaluable patients. In patients positive for anti-Cetuximab antibody, the median time to onset was 44 days (range 8-281 days). Although the number of sero-positive patients is limited, there does not appear to be any relationship between the appearance of antibodies to Cetuximab and the safety or antitumor activity of ERBITUX.

The observed incidence of anti-Cetuximab antibody responses may be influenced by the low sensitivity of available assays, inadequate to reliably detect lower antibody titers. Other factors which might influence the incidence of anti-Cetuximab antibody response include sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to Cetuximab with the incidence of antibodies to other products may be misleading.

Electrolyte Depletion
In 244 patients evaluated in ongoing, controlled clinical trials, the incidence of hypomagnesemia, both overall and severe (NCI-CTC Grades 3 and 4), was increased in patients receiving ERBITUX alone or in combination with chemotherapy as compared to those receiving best supportive care or chemotherapy alone. Approximately one-half of these patients receiving ERBITUX experienced hypomagnesemia and 10-15% experienced severe hypomagnesemia. The onset of electrolyte abnormalities has been reported to occur from days to months after initiation of ERBITUX. Electrolyte repletion was necessary in some patients and in severe cases, intravenous replacement was required. The time to resolution of electrolyte abnormalities is not well known, hence monitoring during and after ERBITUX treatment is recommended. (See **PRECAUTIONS: Laboratory Tests: Electrolyte Monitoring**.)

Infusion Reactions (see BOXED WARNING: Infusion Reactions)
In clinical trials, severe, potentially fatal infusion reactions were reported. These events include the rapid onset of airway obstruction (bronchospasm, stridor, hoarseness), urticaria, and/or hypotension. In major clinical studies in advanced SCCHN, severe infusion reactions (Grade 3 or 4) were observed in 3% of patients receiving ERBITUX plus radiation and 4% of patients receiving ERBITUX monotherapy. In studies in advanced colorectal cancer, severe infusion reactions were observed in 3% of patients receiving ERBITUX plus irinotecan and 2% of patients receiving ERBITUX monotherapy. Grade 1 and 2 infusion reactions, including chills, fever, and dyspnea usually occurring on the first day of initial dosing, were observed in 16% of patients receiving ERBITUX plus irinotecan and 19% of patients receiving ERBITUX monotherapy. (See **WARNINGS: Infusion Reactions** and **DOSAGE AND ADMINISTRATION: Dose Modifications**.)

In the clinical studies described above, a 20-mg test dose was administered intravenously over 10 minutes prior to the loading dose to all patients. The test dose did not reliably identify patients at risk for severe allergic reactions.

Head and Neck Cancer
Except where indicated, the data described below reflect exposure to ERBITUX in 208 patients with locally or regionally advanced SCCHN who received ERBITUX in combination with radiation and as monotherapy in 103 patients with recurrent or metastatic SCCHN. Of the 103 patients receiving ERBITUX monotherapy, 53 continued to a second phase with the combination of ERBITUX plus chemotherapy.

Patients receiving ERBITUX plus radiation therapy received a median of 8 doses (range 1-11 infusions). The population had a median age of 56; 81% were male and 84% Caucasian.

Patients receiving ERBITUX monotherapy, received a median of 11 doses (range 1-45 infusions). The population had a median age of 57; 82% were male and 100% Caucasian.

The most **serious adverse reactions** associated with ERBITUX in combination with radiation therapy in patients with head and neck cancer were:

- Infusion reaction (3%) (see **BOXED WARNINGS**, **WARNINGS**, and **DOSAGE AND ADMINISTRATION: Dose Modifications**);
- Cardiopulmonary arrest (2%) (see **BOXED WARNINGS**, **WARNINGS**);
- Dermatologic toxicity (2.5%) (see **WARNINGS** and **DOSAGE AND ADMINISTRATION: Dose Modifications**);
- Mucositis (6%);
- Radiation dermatitis (3%);
- Confusion (2%);
- Diarrhea (2%).

Fourteen (7%) patients receiving ERBITUX plus radiation therapy and 5 (5%) patients receiving ERBITUX monotherapy, discontinued treatment primarily because of adverse events.

The most common adverse events seen in 208 patients receiving ERBITUX in combination with radiation therapy were acneform rash (87%), mucositis (86%), radiation dermatitis (86%), weight loss (84%), xerostomia (72%), dysphagia (65%), asthenia (56%), nausea (49%), constipation (35%), and vomiting (29%).

The most common adverse events seen in 103 patients receiving ERBITUX monotherapy were acneform rash (76%), asthenia (45%), pain (28%), fever (27%), and weight loss (27%).

The data in Table 1 are based on the experience of 208 patients with locoregionally advanced SCCHN treated with ERBITUX plus radiation therapy compared to 212 patients treated with radiation therapy alone.

Table 1: Incidence of Selected Adverse Events (≥10%) in Patients with Locoregionally Advanced SCCHN

	ERBITUX plus Radiation (n=208)		Radiation Therapy Alone (n=212)	
Body System	**Grades 1-4**	**Grades 3 and 4**	**Grades 1-4**	**Grades 3 and 4**
Preferred Term	% of Patients			
Body as a Whole				
Asthenia	56	4	49	5
Fever[1]	29	1	13	1
Headache	19	<1	8	<1
Infusion Reaction[2]	15	3	2	0
Infection	13	1	9	1
Chills[1]	16	0	5	0
Digestive				
Mucositis/Stomatitis	93	56	94	52
Xerostomia	72	5	71	3
Dysphagia	65	26	63	30
Nausea	49	2	37	2
Constipation	35	5	30	5
Vomiting	29	2	23	4
Anorexia	27	2	23	2
Diarrhea	19	2	13	1
Dyspepsia	14	0	9	1

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Table 1: Incidence of Selected Adverse Events (≥10%) in Patients with Locoregionally Advanced SCCHN *(continued)*

	ERBITUX plus Radiation (n=208)		Radiation Therapy Alone (n=212)	
Body System	**Grades 1-4**	**Grades 3 and 4**	**Grades 1-4**	**Grades 3 and 4**
Preferred Term	% of Patients			
Metabolic/Nutritional				
Weight Loss	84	11	72	7
Dehydration	25	6	19	8
Respiratory				
Pharyngitis	26	3	19	4
Cough Increased	20	<1	19	0
Skin/Appendages				
Acneform Rash[3]	87	17	10	1
Radiation Dermatitis	86	23	90	18
Application Site Reaction	18	0	12	1
Pruritus	16	0	4	0

[1] Includes cases also reported as infusion reaction.
[2] Infusion reaction is defined as any event described at any time during the clinical study as "allergic reaction" or "anaphylactoid reaction", or any event occurring on the first day of dosing described as "allergic reaction", "anaphylactoid reaction", "fever", "chills", "chills and fever", or "dyspnea".
[3] Acneform rash is defined as any event described as "acne", "rash", "maculopapular rash", "pustular rash", "dry skin", or "exfoliative dermatitis".

Late Radiation Toxicity
The overall incidence of late radiation toxicities (any grade) was higher in ERBITUX (Cetuximab) in combination with radiation therapy compared with radiation therapy alone. The following sites were affected: salivary glands (65% versus 56%), larynx (52% versus 36%), subcutaneous tissue (49% versus 45%), mucous membrane (48% versus 39%), esophagus (44% versus 35%), skin (42% versus 33%), brain (11% versus 9%), lung (11% versus 8%), spinal cord (4% versus 3%), and bone (4% versus 5%). The incidence of Grade 3 or 4 late radiation toxicities were generally similar between the radiation therapy alone and the ERBITUX plus radiation treatment groups.

Colorectal Cancer
Except where indicated, the data described below reflect exposure to ERBITUX in 774 patients with advanced metastatic colorectal cancer. ERBITUX was studied in combination with irinotecan (n=354) or as monotherapy (n=420). Patients receiving ERBITUX plus irinotecan received a median of 12 doses [with 88/354 (25%) treated for over 6 months], and patients receiving ERBITUX monotherapy received a median of 7 doses [with 36/420 (9%) treated for over 6 months]. The population had a median age of 59 and was 59% male and 91% Caucasian. The range of dosing for patients receiving ERBITUX plus irinotecan was 1-84 infusions, and the range of dosing for patients receiving ERBITUX monotherapy was 1-63 infusions.

The most **serious adverse reactions** associated with ERBITUX were:

- Infusion reaction (3%) (see **BOXED WARNING**, **WARNINGS**, and **DOSAGE AND ADMINISTRATION: Dose Modifications**);
- Dermatologic toxicity (1%) (see **WARNINGS** and **DOSAGE AND ADMINISTRATION: Dose Modifications**);
- Interstitial lung disease (0.4%) (see **WARNINGS**);
- Fever (5%);
- Sepsis (3%);
- Kidney failure (2%);
- Pulmonary embolus (1%);
- Dehydration (5%) in patients receiving ERBITUX plus irinotecan, 2% in patients receiving ERBITUX monotherapy;
- Diarrhea (6%) in patients receiving ERBITUX plus irinotecan, 0.2% in patients receiving ERBITUX monotherapy.

Thirty-seven (10%) patients receiving ERBITUX plus irinotecan and 17 (4%) patients receiving ERBITUX monotherapy discontinued treatment primarily because of adverse events.

The most common adverse events seen in 354 patients receiving ERBITUX plus irinotecan were acneform rash (88%), asthenia/malaise (73%), diarrhea (72%), nausea (55%), abdominal pain (45%), and vomiting (41%).

The most common adverse events seen in 420 patients receiving ERBITUX monotherapy were acneform rash (90%), asthenia/malaise (48%), nausea (29%), fever (27%), constipation (26%), abdominal pain (26%), headache (26%), and diarrhea (25%).

Data in patients with advanced colorectal carcinoma in Table 2 are based on the experience of 354 patients treated with ERBITUX plus irinotecan and 420 patients treated with ERBITUX monotherapy.

Table 2: Incidence of Adverse Events (≥10%) in Patients with Advanced Colorectal Carcinoma

	ERBITUX plus Irinotecan (n=354)		ERBITUX Monotherapy (n=420)	
Body System	**Grades 1-4**	**Grades 3 and 4**	**Grades 1-4**	**Grades 3 and 4**
Preferred Term[1]	% of Patients			
Body as a Whole				
Asthenia/Malaise[2]	73	16	48	10
Abdominal Pain	45	8	26	9
Fever[3]	34	4	27	<1
Pain	23	6	17	5
Infusion Reaction[4]	19	3	21	2
Infection	16	1	14	1
Back Pain	16	3	10	2
Headache	14	2	26	2
Digestive				
Diarrhea	72	22	25	2
Nausea	55	6	29	2
Vomiting	41	7	25	3
Anorexia	36	4	23	2
Constipation	30	2	26	2
Stomatitis	26	2	10	<1
Dyspepsia	14	0	6	0
Hematic/Lymphatic				
Leukopenia	25	17	<1	0
Anemia	16	5	9	3
Metabolic/Nutritional				
Weight Loss	21	0	7	1
Peripheral Edema	16	1	10	1
Dehydration	15	6	10	3
Nervous				
Insomnia	12	0	10	<1
Depression	10	0	7	0

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ScriptDoctor

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had left his poor Chicago neighborhood, gained an education and a medical degree; but he had lost the ability to connect with people who were once his neighbors.

"And then a patient navigator was brought in who started to get through to her. It was somebody like her from the community, who had cancer that had spread to the bone and was in remission three years out," Dr. Sachs says. "And that clip worked dramatically for Pratt, who is educated and smart, to have to confront some of these beliefs."

Dr. Sachs had latched onto the cancer myths and patient navigator concepts brought to him by a New York City oncologist because of their dramatic potential. It was a bonus that the *ER* episode then echoed from Los Angeles back to Washington, DC.

'Remarkable Circle'

"So that's a remarkable circle of that story, starting with the kernel of an idea from a briefing about the fact that there are differences in cancer statistics in the inner city and in more suburban areas, talking to the expert, Dr. Harold Freeman, coming up with a compelling dramatic story for Pratt and then, as a side effect, having it result in the passage of congressional legislation that's going to affect millions of people. That's a cool story," Dr. Sachs says.

Licy DoCanto says that of course many people worked on many efforts over several years to win federal funding for patient navigator programs, such as Gilbert H. Friedell, MD, at the University of Kentucky Cancer Center, who could show that the problems weren't restricted to big cities. But the *ER* episode came along at the right time, and it dovetailed with other media outreach, such as Dr. Freeman's work with the Ralph Lauren Center and Spanish-language radio programs done by Elmer E. Huerta, MD, MPH, of Washington Cancer Institute.

"The media, without a doubt, was critical as an influence," DoCanto says.

Staffers Who Worked on the Legislation Credit the Show with Helping to Raise Awareness

Representative (now Senator) Bob Menendez (D-NJ) sponsored the House bill to fund patient navigator programs. His spokesman, Allyn Brooks-LaSure, says that staffers who worked on the legislation credit the *ER* clips with helping to raise awareness.

"They didn't see any sort of direct

Table 2: Incidence of Adverse Events (≥10%) in Patients with Advanced Colorectal Carcinoma *(continued)*

	ERBITUX plus Irinotecan (n=354)		ERBITUX Monotherapy (n=420)	
Body System	**Grades 1-4**	**Grades 3 and 4**	**Grades 1-4**	**Grades 3 and 4**
Preferred Term[1]	% of Patients			
Respiratory				
Dyspnea[3]	23	2	17	7
Cough Increased	20	0	11	1
Skin/Appendages				
Acneform Rash[5]	88	14	90	8
Alopecia	21	0	4	0
Skin Disorder	15	1	4	0
Nail Disorder	12	<1	16	<1
Pruritus	10	1	11	<1
Conjunctivitis	14	1	7	<1

[1] Adverse events that occurred (toxicity Grades 1 through 4) in ≥10% of patients with refractory colorectal carcinoma treated with ERBITUX (Cetuximab) plus irinotecan or in ≥10% of patients with refractory colorectal carcinoma treated with ERBITUX monotherapy.
[2] Asthenia/malaise is defined as any event described as "asthenia", "malaise", or "somnolence".
[3] Includes cases also reported as infusion reaction.
[4] Infusion reaction is defined as any event described at any time during the clinical study as "allergic reaction" or "anaphylactoid reaction", or any event occurring on the first day of dosing described as "allergic reaction", "anaphylactoid reaction", "fever", "chills", "chills and fever", or "dyspnea".
[5] Acneform rash is defined as any event described as "acne", "rash", "maculopapular rash", "pustular rash", "dry skin", or "exfoliative dermatitis".

Dermatologic Toxicity and Related Disorders
Non-suppurative acneform rash described as "acne", "rash", "maculopapular rash", "pustular rash", "dry skin", or "exfoliative dermatitis" was observed in patients receiving ERBITUX plus radiation, ERBITUX plus irinotecan, or ERBITUX monotherapy. One or more of the dermatological adverse events were reported in 87% (17% Grade 3 or 4) of patients receiving ERBITUX plus radiation and in 76% (1% Grade 3 or 4) receiving ERBITUX monotherapy during treatment for advanced SCCHN. In studies of advanced colorectal cancer, dermatological adverse events were reported in 88% (14% Grade 3) of patients receiving ERBITUX plus irinotecan and in 90% (8% Grade 3) of patients receiving ERBITUX monotherapy. Acneform rash most commonly occurred on the face, upper chest, and back, but could extend to the extremities and was characterized by multiple follicular- or pustular-appearing lesions. Skin drying and fissuring were common in some instances, and were associated with inflammatory and infectious sequelae (eg, blepharitis, cellulitis, cyst). Two cases of *S. aureus* sepsis were reported. The onset of acneform rash was generally within the first two weeks of therapy. Although in a majority of the patients the event resolved following cessation of treatment, in nearly half of the cases, the event continued beyond 28 days. (See **WARNINGS: Dermatologic Toxicity** and **DOSAGE AND ADMINISTRATION: Dose Modifications**.)

A related nail disorder, occurring in 12% of patients (0.4% Grade 3), was characterized as a paronychial inflammation with associated swelling of the lateral nail folds of the toes and fingers, with the great toes and thumbs as the most commonly affected digits.

OVERDOSAGE
Single doses of ERBITUX higher than 500 mg/m^2 have not been tested. There is no experience with overdosage in human clinical trials.

DOSAGE AND ADMINISTRATION
General
Premedication with an H_1 antagonist (eg, 50 mg of diphenhydramine IV) is recommended. Appropriate medical resources for the treatment of severe infusion reactions should be available during ERBITUX infusions. (See **WARNINGS: Infusion Reactions**.)

Squamous Cell Carcinoma of the Head and Neck
The recommended dose of ERBITUX, in combination with radiation therapy is 400 mg/m^2 as an initial loading dose (first infusion) administered as a 120-minute IV infusion (maximum infusion rate 5 mL/min) one week prior to initiation of a course of radiation therapy. The recommended weekly maintenance dose (all other infusions) is 250 mg/m^2 infused over 60 minutes (maximum infusion rate 5 mL/min) weekly for the duration of radiation therapy (6-7 weeks). In clinical studies, Cetuximab was administered 1 hour prior to radiation therapy.

The recommended dosing regimen for single-agent ERBITUX in the treatment of recurrent or metastatic squamous cell carcinoma of the head and neck is a 400-mg/m^2 initial dose followed by 250 mg/m^2 weekly until disease progression or unacceptable toxicity.

Colorectal Cancer
The recommended dose of ERBITUX, in combination with irinotecan, or as monotherapy, is 400 mg/m^2 as an initial loading dose (first infusion) administered as a 120-minute IV infusion (maximum infusion rate 5 mL/min). The recommended weekly maintenance dose (all other infusions) is 250 mg/m^2 infused over 60 minutes (maximum infusion rate 5 mL/min).

Dose Modifications
Infusion Reactions
If the patient experiences a mild or moderate (Grade 1 or 2) infusion reaction, the infusion rate should be permanently reduced by 50%.

ERBITUX (Cetuximab) should be immediately and permanently discontinued in patients who experience severe (Grade 3 or 4) infusion reactions. (See **WARNINGS** and **ADVERSE REACTIONS**.)

Dermatologic Toxicity and Related Disorders
Dosage modifications for dermatologic toxicity are recommended for severe acneform rash (NCI CTC Grades 3 or 4), as specified in Table 3. ERBITUX dosage modification is not recommended for severe radiation dermatitis. (See **WARNINGS** and **ADVERSE REACTIONS**.)

Table 3: ERBITUX Dose Modification Guidelines

Severe Acneform Rash	ERBITUX	Outcome	ERBITUX Dose Modification
1st occurrence	Delay infusion 1 to 2 weeks	Improvement No Improvement	Continue at 250 mg/m^2 Discontinue ERBITUX
2nd occurrence	Delay infusion 1 to 2 weeks	Improvement No Improvement	Reduce dose to 200 mg/m^2 Discontinue ERBITUX
3rd occurrence	Delay infusion 1 to 2 weeks	Improvement No Improvement	Reduce dose to 150 mg/m^2 Discontinue ERBITUX
4th occurrence	Discontinue ERBITUX		

Manufactured by ImClone Systems Incorporated, Branchburg, NJ 08876
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AstraZeneca Giving $10 Million to ACS Patient Navigator Program

As *OT* went to press, AstraZeneca and the American Cancer Society announced a collaboration to significantly extend the reach of the Society's Patient Navigator Program.

The company has pledged funding of $10 million to help the ACS develop at least 50 new Patient Navigator Program sites over the next five years. There are currently 60 such sites across the US.

The first new three sites are Seattle Cancer Care Alliance; Helen F. Graham Cancer Center at Christiana Care in Wilmington, DE; and, John H. Stroger Jr. Hospital of Cook County in Chicago.

Harold P. Freeman, MD, Medical Director of the Ralph Lauren Cancer Center in Harlem, NY, who pioneered the concept, said in a statement, "Patient navigators directly assist patients by eliminating financial, communication and emotional barriers to timely diagnosis and treatment. This kind of support may be life saving."

movement as a result of it being included in the episode on television; no specific action or follow-up," Brooks-LaSure says. "But they believe that it was helpful from a practical perspective, because it provided a tangible example of exactly how the patient navigator program would work—sort of a tool to be able to point people to."

Personal Interest from CNN Work 15 Years Ago

Does a dramatic story have a different sort of persuasive power than standard hearing testimony or a straight factual report, such as a news story? That's where my personal interest in this episode of health care legislative lobbying comes in. You see, I did a series of reports on cancer in poor communities that included Dr. Freeman and showed a patient navigator at work. That series aired on CNN 15 years ago. I'm not aware that the stories produced any movement on related health care policy.

Maybe it was a confluence of factors that led to federal funding for patient navigator programs just months after they were mentioned on *ER*. But I think that at the very least, the show was a bellwether of popular attitudes. The way that the patient navigator was portrayed indicated that the mood had

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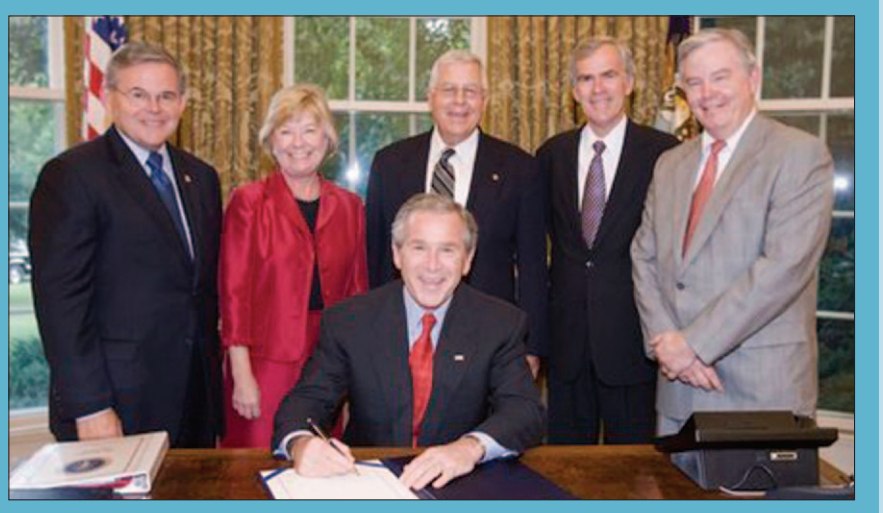

President Bush signing into law HR 1812, the "Patient Navigator Outreach and Chronic Disease Prevention Act of 2005," which authorized appropriations through FY 2010 for the Department of Health and Human Services to establish a competitive grant program designed to help patients access health care services. Shown here with President Bush in the Oval Office on June 29, 2005, are (left to right) Congressman Bob Menendez (D-NJ), Congresswoman Deborah Pryce (R-OH), Senator Mike Enzi (R-WY), Senator Jeff Bingaman (D-NM), and Congressman Joe Barton (R-TX).

Good News & Bad News from 20-Year Follow-Up of AML Survivors

By Naomi Pfeiffer

ORLANDO—If youngsters with acute myeloid leukemia (AML) survive the first five years after diagnosis, they are very likely to survive for a long life. But the quality of that life may be problematic.

That was the conclusion of study of a cohort of young AML survivors followed for 20 years, reported here at the American Society of Hematology Annual Meeting

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AML now accounts for approximately 25% of childhood leukemias, with an increased incidence in teenagers and young adults, noted the lead researcher, Daniel A. Mulrooney MD, Assistant Professor at the University of Minnesota Medical School.

"The survival rates are wonderful," he said in presenting the results. Among the five-year survivors, 97% were still alive 10 years later and 94% were alive after 20 years (25 years after diagnosis). "A colleague called these overall survival data one of the great success stories of clinical oncology," Dr. Mulroney said.

"We call the emergence of these illnesses 'late medical effects,' but in a normal population they would be seen as alarmingly early effects."

"At the same time, however, we found that serious—even life-threatening—illnesses appeared many years later in these aggressively treated patients."

In fact, he emphasized in his oral presentation, the incidence and severity of second cancers and heart disease in particular—as well as other troubling conditions due to the original cancer treatment—seemed to increase with time.

He urged oncologists with AML survivors as patients to start monitoring them early and continue monitoring as a routine part of health care because these patients always would be at high risk.

"It is crucial that they be evaluated for life in a long-term follow-up clinic, where a physician familiar with the unique issues of cancer survivors can review their prior treatment and screen for late effects of cancer therapy," he said.

Multiple Quality-of-Life Factors

The study is a first-ever look into quality-of-life factors such as education, employment, and marriage among AML survivors compared with a sibling control group and the general population. The investigators—all pediatric cancer specialists—evaluated 272 AML survivors (55% female) enrolled in the Childhood Cancer Survivor Study, a retrospective cohort study that tracks the health status of adults diagnosed with various childhood cancers between 1970 and 1986.

To take part in the AML investigation, survivors had to have lived at least five years after diagnosis, have been younger than 21 at diagnosis, and have never received treatment with a blood or marrow transplant (due to reports about the unfavorable consequences of total body irradiation). The average age at follow-up was about 22.

"We call the emergence of these illnesses 'late medical effects,' but in a normal population they would be seen as alarmingly early effects."

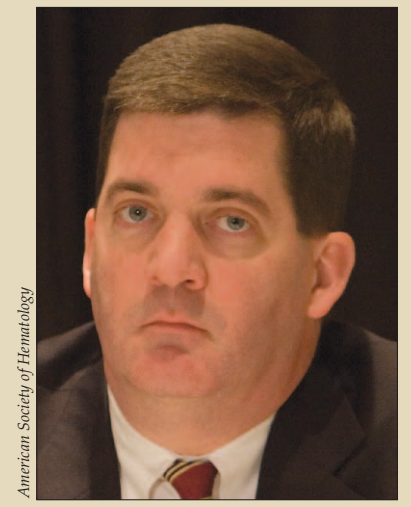
Among the five-year survivors studied, six reported disease recurrences, two died from relapse, one from congestive heart failure, and one from a myocardial infarction. The incidence of recurring AML was 1.8% at 10 years and 3.7% at 20 years.

Like several other recent reports on childhood cancer survivors, the AML study suggests that early therapy with high-dose anthracyclines—as well as radiation—is largely responsible for the gradual deterioration of cardiac function and the reappearance of cancer in these young people.

Approximately 56% of the AML study subjects received chemotherapy only, and 34% had both chemotherapy and radiation.

"Adriamycin in particular has been shown to involve many cardiac structures," Dr. Mulrooney said, adding that AML survivors who were treated with certain families of drugs such as anthracyclines will virtually always be at risk.

"Signs of cardiac disease and/or second cancers may show up 20 or 30 years after diagnosis. Many clinicians are still unaware that these wonderful drugs—so successful in promoting longer life—can also cause high morbidity later on."



American Society of Hematology

Daniel A. Mulrooney, MD: "The survival rates are wonderful—A colleague called these overall survival data one of the great success stories of clinical oncology. At the same time, however, we found that serious—even life-threatening—illnesses appeared many years later in these aggressively treated patients....It is crucial that they be evaluated for life in a long-term follow-up clinic, where a physician familiar with the unique issues of cancer survivors can review their prior treatment and screen for late effects of cancer therapy."

Endocrine System Dysfunction

Additionally, the research team looked at chronic health conditions in the young survivors and found that—as previously shown—the most worrisome involved endocrine system dysfunction as well as progressive cardiomyopathies and repeat malignancies.

About 16% had a severe or chronic—but treatable—condition such as renal dysfunction or osteoporosis compared with 6% in the siblings.

Additionally, new studies—notably a poster study on ALL survivors presented at the ASH meeting (*Abstract 1833*)—report that chronic painful musculoskeletal conditions also are showing up later in life, limiting physical functioning and daily activities, he said.

In contrast, on social outcomes, the data show that AML survivors did remarkably well as adults, he said. Among those 25 years or older, marriage rates were similar between the survivors and the general American population at 59%, but lower compared with the sibling comparison group at 69%; divorce rates also were lower.

Educational attainment was "terrific," particularly considering the survivors' history, Dr. Mulrooney said. "Some early studies had suggested they tended to do poorly in school, setting them up for low expectations. We looked at AML survivors who had received only chemotherapy as well as those receiving both chemo and radiation. They all did about the same in grade school and college. The survivors' rate of college graduation was 44% compared with the siblings' 52%, but was higher than the 34% reported for the general population."

All survivors and siblings were employed, and most had health insurance (93% vs 90%).

'Our Job is Educational'

Asked for his opinion, Rajaram Nagarajan, MD, Assistant Professor in the Division of Hematology/Oncology/BMT at Cincinnati Children's Hospital Medical Center, who was not involved in the study, called the information encouraging and said, "As a pediatric oncologist, I sometimes find it difficult to experience 'the fruits of our labor' since many survivors are lost to follow-up as adults. In this case, I was gratified to encounter such positive outcomes in the survivors despite the intensive therapy they received.

"This study should remind us that while childhood cancer survivors can do well after therapy, we must be vigilant about them over the long term."

"However, it is sobering to realize that problems such as heart disease and secondary neoplasms can appear decades after treatment. Additionally, although many late effects are caused by radiation therapy, it's important to note that many others may occur in survivors not treated with radiation. This study should remind us that while childhood cancer survivors can do well after therapy, we must be vigilant about them over the long term. Our job is educational: to educate not only the survivors, but also their families and primary care physicians about the threat, perhaps even the inevitability, of the late effects of cancer treatment and the need for appropriate follow-up."

ScriptDoctor

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shifted from "What are they? Why do we need them?" to "Oh, of course, let's get more of them now."

And so, now more patient navigators are on the way.

Next time: "It's Only TV"—evidence that entertainment messages have an effect.