



SCRIPTDOCTOR: MEDICINE IN THE MEDIA

Medicine in a Musical

By Andrew Holtz, MPH

The story of a physician who is nearly consumed by temptation made headlines in the *New York Times*—show biz headlines, that is. On the heels of *Oklahoma!* and *Carousel*, Richard Rodgers and Oscar Hammerstein II had \$500,000 worth of ticket sales already in the till on the day *Allegro* opened on Broadway at the Majestic Theatre.

It was October 10, 1947. Sam Zolotow, theater reporter for the *Times*, wrote that despite unprecedented advance sales (\$500,000 in 1947 is the equivalent of \$5 million today), the thirst for tickets could not be slaked: “Prospective customers have raised a hue and cry because they haven’t been able to get tickets. From personal observation, we can assure them that strenuous efforts are being made to please all. They’ll have to be patient, though, as the demand has assumed flood-like proportions,” he wrote.

And yet the next morning, reviews were mixed. Some were sharply negative. Today, *Allegro* is largely unknown and rarely staged.

But back to the reason for writing about this six-decade-old show: It’s all

about the life of a physician, Joseph Taylor Jr., the son of a small-town doctor. I discovered this episode of medicine in the musicals through an article

by historian of medicine Howard Markel, MD, PhD, writing in the *Journal of the American Medical Association* (“Gotta’ Sing! Gotta’ Diagnose!” A

Postmortem Examination of Rodgers and Hammerstein’s Medical Musical Allegro. *JAMA* 2007;298:1575-1577).

A fan of musicals, Dr. Markel says

Now Approved

IXEMPRA™

(ixabepilone) for injection

IXEMPRA is indicated as monotherapy for the treatment of metastatic or locally advanced breast cancer in patients whose tumors are resistant or refractory to anthracyclines, taxanes, and capecitabine.

IXEMPRA is indicated in combination with capecitabine for the treatment of patients with metastatic or locally advanced breast cancer resistant to treatment with an anthracycline and taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated. Anthracycline resistance is defined as progression while on therapy or within 6 months in the adjuvant setting or 3 months in the metastatic setting. Taxane resistance is defined as progression while on therapy or within 12 months in the adjuvant setting or 4 months in the metastatic setting.

For additional information, please call 1-888-IXEMPRA (493-6772) or visit www.IXEMPRA.com



Howard Markel, MD, PhD, who wrote an article about *Allegro* in a recent issue of *JAMA*, said that although on every level medicine has changed markedly since 1947 when the show opened, “that’s the great thing about a classic, that any great work of art or literature continues to speak to generations long after the day-to-day details it describes have become antiquated.”

he had picked up a copy of the *Allegro* script when he was a teenager, but just tucked it away. Then during a visit to New York, he listened to a rare cast recording from the production.

"It just jumped out as, 'Yes, this needs to be written about!' so I did," he said.

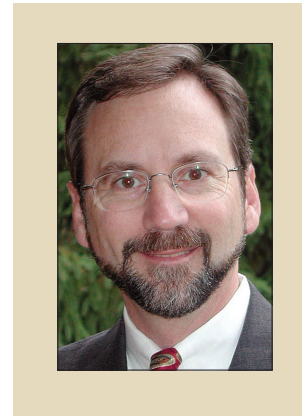
In the show, young Dr. Taylor aspired to help his father realize a dream of expanding the three-bed hospital attached to their home. But his new wife has grander ambitions. She maneuvers her husband into accepting a prominent position at a big-city prac-

tice. Instead of caring for farmers and their families, the doctor finds himself catering to the foibles of the worried wealthy. Bedside manner is supplanted by cocktail party prattle.

Dr. Markel sees eternal themes in this medical storyline: "What were your original goals? Why did you go into medicine? Or, why did you choose a particular branch of medicine? Or, why did you choose practice over academia? And more broadly, as we talk to our patients, what choices are they making?"

In the preface to a published ver-

sion of the script, Oscar Hammerstein wrote that an equivalent story could be told about other professions. Yet he noted the ways he saw the practice of medicine warped by money and celebrity. I think it's telling that Hammerstein felt that a physician so neatly fit the bill of a character diverted from his intended path by nudges and lures.



Andrew Holtz, MPH, is a former CNN Medical Correspondent and the author of "The Medical Science of House, M.D." Send questions to him about how the media treat medical topics or suggestions for future columns to OT@lwwny.com

"It is difficult for a man to recog-
(continued on page 50)

Important Safety Information

Toxicity in hepatic impairment

- ▶ **KEYTRUDA (pembrolizumab) in combination with cyclophosphamide is contraindicated in patients with AST or ALT >2.5 x ULN or bilirubin >1 x ULN due to increased risk of toxicity and neutropenia-related death.**
- ▶ In combination with oprelvekin, the overall frequency of grade 3/4 adverse reactions, febrile neutropenia, serious adverse reactions, and toxicity-related deaths was greater in patients with hepatic impairment.
- ▶ Caution should be used when using KEYTRUDA as monotherapy in patients with AST or ALT >5 x ULN. Use of KEYTRUDA in patients with AST or ALT >10 x ULN or bilirubin >3 x ULN is not recommended.
- ▶ With monotherapy, grade 4 neutropenia, febrile neutropenia, and serious adverse reactions were more frequent in patients with hepatic impairment.

Contraindications

- ▶ KEYTRUDA is contraindicated in patients:
 - with a known history of a severe (CTC grade 3/4) hypersensitivity reaction to agents containing Cremophor[®] EL or its derivatives such as polyoxyethylated castor oil
 - who have a baseline neutrophil count <1500 cells/mm³ or a platelet count <100,000 cells/mm³

Peripheral neuropathy

- ▶ Patients treated with KEYTRUDA should be monitored for symptoms of neuropathy, such as burning sensation, hyperesthesia, hypoesthesia, paresthesia, discomfort, or neuropathic pain. Patients experiencing new or worsening peripheral neuropathy may require changes in the dose or discontinuation of KEYTRUDA. Neuropathy was the most frequent cause of treatment discontinuation due to drug toxicity. Caution should be used when treating patients with diabetes mellitus or existing intolerant to severe neuropathy.

Myelosuppression

- ▶ Patients should be monitored for myelosuppression; frequent peripheral blood cell counts are recommended for all patients receiving KEYTRUDA.
- ▶ Patients who experience severe neutropenia or thrombocytopenia should have their dose reduced. Neutropenia-related deaths occurred in patients administered KEYTRUDA and oprelvekin (1.5% of 44 patients) and KEYTRUDA alone (0.4% in 240 patients).

Hypersensitivity reactions

- ▶ Premedicate with an H₁ and an H₂ antagonist approximately 1 hour before KEYTRUDA (pembrolizumab) infusion and observe for hypersensitivity reactions (e.g., flushing, rash, dyspnea, and bronchospasm).
- ▶ In case of severe hypersensitivity reactions, infusion of KEYTRUDA should be stopped and aggressive supportive treatment (e.g., epinephrine, corticosteroids) started.
- ▶ Patients who experience a hypersensitivity reaction in one cycle of KEYTRUDA must be premedicated in subsequent cycles with a corticosteroid in addition to the H₁ and H₂ antagonists, and extension of the infusion time should be considered.

Pregnancy

- ▶ Women should be advised not to become pregnant when taking KEYTRUDA. If this drug is used during pregnancy or the patient becomes pregnant, the patient should be apprised of the potential hazard to the fetus.

Cardiac adverse reactions

- ▶ Caution should be exercised in patients with a history of cardiac disease. Discontinuation of KEYTRUDA should be considered in patients who develop cardiac ischemia or impaired cardiac function due to reports of cardiovascular adverse reactions (e.g., myocardial ischemia, supraventricular arrhythmia, and ventricular dysfunction). The frequency of cardiac adverse reactions (myocardial ischemia and ventricular dysfunction) was higher in the KEYTRUDA in combination with oprelvekin (1.5%) than in the oprelvekin alone (0.5%) treatment group.

Potential for cognitive impairment from excipients

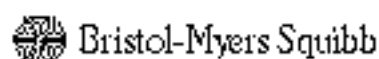
- ▶ KEYTRUDA contains 1-decylmethyl alcohol USP. Consideration should be given to the possibility of central nervous system and other effects of alcohol.

Adverse reactions

- ▶ The most common adverse reactions (≥20%) reported by patients receiving KEYTRUDA were peripheral sensory neuropathy, fatigue/asthenia, myalgia/arthralgia, alopecia, nausea, vomiting, stomatitis, mucositis, diarrhea, and musculoskeletal pain. The following additional events occurred in ≥20% in combination treatment (pain-in-plantar erythrodysaesthesia [burnt-foot) syndrome, anorexia, abdominal pain, nail disorder, and constipation. Drug-associated hematologic abnormalities (≥4%) include neutropenia, leukopenia, anemia, and thrombocytopenia.

Cremophor is a registered trademark of BASF AG.

Please see brief summary on following pages, including boxed **WARNING** regarding hepatic impairment.



Script Doctor

continued from page 49

nize the gentle transitions of his own deterioration....” Hammerstein wrote in that preface. What a delicious construction of words! Say it aloud and the phrase echoes with a feeling of stealthy, inexorable corruption.

He continues: "...the millions of small steps whereby he becomes less and less a doctor, more and more a politician, a promoter, a rumba dancer, a cocktail-party raconteur, a wet-nurse

“When you open the ‘Allegro’ time capsule to see how popular media of the mid-20th century portrayed physicians and the practice of medicine, the essential message about tension between professional ideals and common reality remains solidly familiar.”

for spoiled adults—everything but what he started out to be, studied to be, struggled to be.”

All it would take is the insertion of “well-paid device companies” for this com-

ment, penned more than a half-century ago, to seem to be an op-ed on medical conflicts of interest cut from today’s newspaper.

Dr. Markel notes that in the decades since *Allegro* premiered, medicine has changed more than it had in preceding centuries. A multitude of effective treatments are common now that were beyond the science fiction of the mid-20th century. The transformation in medical devices and methods is illustrated by a bit of period technology featured in a turning point in the drama.

Dr. Taylor is entertaining guests

EXEMPRA™ Kit (ceftaroline) for Injection, for intravenous infusion only

Exemplar Pharmaceuticals, Inc. For complete prescribing information see full prescribing information.

WARNING: RISK OF ANAPHYLACTIC REACTION
EXEMPRA is contraindicated in patients with a history of anaphylactic reaction to any beta-lactam antibiotic. Patients with a history of anaphylactic reaction to any beta-lactam antibiotic should be monitored closely for signs and symptoms of anaphylaxis.

INDICATIONS AND USAGE
EXEMPRA is indicated for the treatment of acute bacterial sinusitis in patients with a history of sinusitis. EXEMPRA is also indicated for the treatment of acute bacterial sinusitis in patients with a history of sinusitis who are allergic to penicillins and cephalosporins. EXEMPRA is also indicated for the treatment of acute bacterial sinusitis in patients with a history of sinusitis who are allergic to penicillins and cephalosporins.

CONTRAINDICATIONS
EXEMPRA is contraindicated in patients with a history of anaphylactic reaction to any beta-lactam antibiotic. Patients with a history of anaphylactic reaction to any beta-lactam antibiotic should be monitored closely for signs and symptoms of anaphylaxis.

WARNINGS AND PRECAUTIONS
Patients should be monitored for signs and symptoms of anaphylaxis. Patients with a history of anaphylactic reaction to any beta-lactam antibiotic should be monitored closely for signs and symptoms of anaphylaxis. Patients with a history of anaphylactic reaction to any beta-lactam antibiotic should be monitored closely for signs and symptoms of anaphylaxis.

Table 1: Treatment of Acute Bacterial Sinusitis (ABSSIM) Study

	EXEMPRA (n=101)	EXEMPRA (n=101)
Patients completing the study	97%	97%
Patients completing the study with a clinical response	97%	97%
Patients completing the study with a clinical response and a laboratory response	97%	97%
Patients completing the study with a clinical response and a laboratory response and a patient satisfaction score	97%	97%

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

97% and 97% of patients in the EXEMPRA and EXEMPRA groups, respectively, completed the study.

Table 2: Treatment of Acute Bacterial Sinusitis (ABSSIM) Study

System Organ Class	EXEMPRA (n=101)		EXEMPRA (n=101)	
	Total (%)	Control (%)	Total (%)	Control (%)
Headache	4	0	5	0
Nausea	5	4*	1	1*
Dizziness	2	1*	0	0
Diarrhea	5	5*	1*	1*
Stomach pain	5	2	2	2
Constipation	0	<1*	2	0
Abdominal pain	5	2	1	1
Flatulence	5	2	2	2
Indigestion	5	2	2	2
Extraneous taste	5	2	2	2
Altered taste	5	2	2	2
Excessive sweating	5	2	2	2
Pruritus	5	2	2	2
Rhinitis	5	2	2	2
Sinusitis	5	2	2	2
Upper respiratory tract infection	5	2	2	2
Pharyngitis	5	2	2	2
Stomatitis	5	2	2	2
Yeast infection	5	2	2	2
Other	5	2	2	2

* p < 0.05 compared to control. Percentages are based on the number of patients who completed the study. Percentages are based on the number of patients who completed the study.

(described as "high-bracket patients, and hospital trustees") when he is interrupted by his nurse. She's brought along x-ray films of a less-prominent patient's stomach. The doctor had hastily reviewed the films before dashing off to the party.

"But I've already looked at them. You were there, Emily. Don't you remember? I told you to phone him and tell him there was nothing to worry about," Dr. Taylor chides.

But the nurse persists, pointing to a spot on the film. "Couldn't that be an ulcer crater?"

Dr. Taylor's wife, Jenny, enters and urges him back to the party. One of his benefactors is calling for him. Jenny Taylor tells the nurse, "She wants to talk to my husband about donating three hundred thousand dollars toward our new private pavilion." That'd be about \$3 million today.

Dr. Taylor hustles back into the party, but he realizes his quick first reading of the film was wrong.

Dr. Markel says that on one hand, the scene illustrates how much has changed in medicine.

"This guy was using a flat plate

belly film to diagnose a peptic ulcer. In 1947 that was kind of cutting edge. We use very different methods today."

The treatments are different, too: "In 1947 you basically did a Billroth II, you surgically remove half the stomach, and that created a dumping syndrome—as opposed to now, with all the wonderful acid reflux reducers that we have."

And yet on the other hand, it reveals how much the song remains the same.

"So on every level medicine has changed markedly, but that's the great



thing about a classic, and that's an overused word, but to me any great work of art or literature continues to speak to generations long after the day-to-day details it describes have become antiquated," Dr. Markel said.

When you open the *Allegro* time capsule to see how popular media of the mid-20th century portrayed physicians and the practice of medicine, the essential message about tension between professional ideals and common reality remains solidly familiar.

Medical School Enrollment Increases; More Black & Hispanic Males Apply

Association of American Medical Colleges data show that the 2007 class is the largest in history. The number of first-year enrollees is almost 17,800, a 2.3% increase over 2006. More than 42,300 people applied in 2007, an 8.2% increase over last year.

The 2007 applicants included more people from racial and ethnic minorities. Black and Hispanic male applicants increased by 9.2%, and black males accepted and enrolled this fall increased by 5.3%. The number of Hispanic male first-year entrants was the same as in 2006.

"With our nation expected to face a serious shortage of physicians in the future, we are pleased to see interest in medicine continuing to increase," AAMC President Darrell G. Kirch, MD, said. "We are especially encouraged by the growing interest among students from groups historically underrepresented in medicine."

Overall, the academic credentials of applicants to medical schools this year were stronger than ever, with the highest MCAT scores and cumulative grade point averages on record. In addition, over the past five years there has been an increase in applicants' average amount of experience in premedical activities, including time spent in medical research and community service in clinical and nonclinical settings.

Table 2: Baseline Characteristics of the Study Cohort by Study Group

Characteristic	Study (A)				Study (B)	
	Mean (SD)	Median (IQR)	Range	Range	Mean (SD)	Median (IQR)
Age at Enrollment (years)	58	58	45-80	45-80	58	58
Age at Baseline (years)	60	60	45-80	45-80	60	60
Sex (Male/Female)	200/100	200/100			200/100	200/100
Race (White/Black/Hispanic)	150/30/20	150/30/20			150/30/20	150/30/20
Ethnicity (Hispanic)	20	20			20	20
Education (College/Postgraduate)	120/80	120/80			120/80	120/80
Employment (Full-time/Part-time)	100/100	100/100			100/100	100/100
Health Insurance (Medicare/Medicaid/Private)	100/100	100/100			100/100	100/100
Comorbidities (Hypertension/Diabetes/Cholesterol)	100/100	100/100			100/100	100/100

Baseline characteristics of the study cohort by study group. The study cohort was well-matched for demographic and clinical characteristics. Key variables include age, sex, race, ethnicity, education, employment, health insurance, and comorbidities. The study design is a randomized controlled trial comparing two treatment arms (Study A and Study B). The primary outcome is the rate of major adverse cardiovascular events (MACE).

Table 3: Baseline Characteristics of the Study Cohort by Study Group

Characteristic	Study (A)				Study (B)	
	Mean (SD)	Median (IQR)	Range	Range	Mean (SD)	Median (IQR)
Age at Enrollment (years)	58	58	45-80	45-80	58	58
Age at Baseline (years)	60	60	45-80	45-80	60	60
Sex (Male/Female)	200/100	200/100			200/100	200/100
Race (White/Black/Hispanic)	150/30/20	150/30/20			150/30/20	150/30/20
Ethnicity (Hispanic)	20	20			20	20
Education (College/Postgraduate)	120/80	120/80			120/80	120/80
Employment (Full-time/Part-time)	100/100	100/100			100/100	100/100
Health Insurance (Medicare/Medicaid/Private)	100/100	100/100			100/100	100/100
Comorbidities (Hypertension/Diabetes/Cholesterol)	100/100	100/100			100/100	100/100

Baseline characteristics of the study cohort by study group. The study cohort was well-matched for demographic and clinical characteristics. Key variables include age, sex, race, ethnicity, education, employment, health insurance, and comorbidities. The study design is a randomized controlled trial comparing two treatment arms (Study A and Study B). The primary outcome is the rate of major adverse cardiovascular events (MACE).

The study cohort was well-matched for demographic and clinical characteristics. Key variables include age, sex, race, ethnicity, education, employment, health insurance, and comorbidities. The study design is a randomized controlled trial comparing two treatment arms (Study A and Study B). The primary outcome is the rate of major adverse cardiovascular events (MACE).

The study cohort was well-matched for demographic and clinical characteristics. Key variables include age, sex, race, ethnicity, education, employment, health insurance, and comorbidities. The study design is a randomized controlled trial comparing two treatment arms (Study A and Study B). The primary outcome is the rate of major adverse cardiovascular events (MACE).

Baseline Characteristics of the Study Cohort by Study Group

The study cohort was well-matched for demographic and clinical characteristics. Key variables include age, sex, race, ethnicity, education, employment, health insurance, and comorbidities. The study design is a randomized controlled trial comparing two treatment arms (Study A and Study B). The primary outcome is the rate of major adverse cardiovascular events (MACE).

Enlighten Company
Pharmaceuticals, LLC
11212 Biscayne Blvd., Suite 1100
Miami, FL 33154
Tel: (305) 555-1234