Quick Comment on *House* about Duke Vaccine Trial Provokes Public Response Bigger than CBS Evening News’ Mention

By Andrew Holtz, MPH

The episode of *House* that aired on Tuesday, March 6 included suspicions that the main character, Dr. Gregory House, might have a brain tumor that could not be successfully treated by conventional therapies. At about 9:33 pm (8:33 pm central and mountain time) the character of Dr. Robert Chase said, “They’ve got another trial going on at Duke. Fifteen percent extend their lives beyond five years. If you are positive you can get the treatment.

That often happens—even though it was mentioned in a fictional setting, people suddenly think, ‘Well, maybe there’s something out there that I don’t know about, and it’s important. So they do start calling up."

One of the most interesting calls, said, was a woman who had a cat with a brain tumor. “She absolutely insisted that we give her cat this vaccine,” he said. “That was probably the oddest call we got.”

The higher-ups at Duke were pleased with the surprise attention. “I was delighted. People all over the country were e-mailing us,” says Henry Friedman, MD, Deputy Director of the Preston Robert Tisch Brain Tumor Center at Duke. He says the primetime plug made them look good to patients and the institution.

“By 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@hoy.com

**Scriptdoctor: Medicine in the Media**

*Before he could finish the sentence, Dr. House cut him short. The brief remark was barely six seconds long. It didn’t mention a specific therapy. But the character did say “Duke.”*

“The next morning people started calling up and saying, ‘They mentioned your vaccine study on *House*.’” recalled John H. Sampson, MD, PhD, Associate Professor of Surgery and Assistant Professor of Pathology at Duke Comprehensive Cancer Center. “Actually they didn’t specifically say it was a vaccine, but I guess that’s what the majority of people took it to mean.”

Dr. Sampson hadn’t seen the show when it first aired, but, boy, did he hear about it. Colleagues and friends called and e-mailed their congratulations that his work was recognized on a hugely popular TV show. Patients and their families wanted to know if they could get the treatment.

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**How Did the Mention Come About?**

But Dr. Friedman had no idea what prompted the mention of Duke brain cancer research, so he called *House* writer Lawrence Kaplow with thanks and a question.

“Why’d you say [Duke]? Especially us over Harvard?” Dr. Friedman asked.

From his end of the conversation, Kaplow recalls Dr. Friedman mentioning the Tisch family, which donated several million dollars to Duke after New York businessman Preston Robert Tisch was treated there. The family also has strong TV connections: Preston Robert’s brother, Laurence, once ran CBS.

“It was so funny,” the *House* writer said about his call with Dr. Friedman. “He was like, ‘Thank you so much for mentioning Duke, we’re talking to the Chairman of Fox, we’re very close with the Tisch family, and obviously Fox has a relationship with Tisch. And it was so nice of Fox to mention Duke.’”

Kaplow then told him the real source of the line: “And I’m like, ‘Fox? Tisch?! No! It’s my friend Michael!’”

Kaplow’s friend was treated at Duke. “He had a Grade IV glioblastoma. He was told at three places that he was gonna die.”

“I was touched that [Friedman] took the time to call up and say thank you. I said there’s no ‘thank you’ necessary. It was just a ‘shout out’ that my friend, who is still alive, would get a kick out of,” Kaplow said.

**‘No Product Placement’**

He said the mention of Duke was not any kind of “product placement,” which he says they carefully avoid in any case. As the storyline involving brain cancer developed, he just wanted to toss in a casual reference to his friend’s brain tumor experience.

“That’s why, when I was researching, I just threw into a Google search ‘What’s Duke doing now?’ You know, give me something crazy that they are doing now. I found one and I mentioned it,” he said.

But in addition to his friend, there were 24 million other viewers watching that episode—some of them with powerful personal reasons to read more than was intended into the mention of Duke’s research.

“In general when patients call, they think we are sort of right around the corner from the breakthrough and the cure. And really that’s not the way it’s going to happen; it’s going to be slow incremental advances,” Dr. Sampson says.

**Starting Phase III Trials**

He said he is confident the therapeutic cancer vaccine they are working on will lead to new treatment options for some patients, but it’s only now entering Phase III trials.

The approach attempts to stimulate an immune system assault on tumor cells with injections of a variant of epidermal growth factor receptor protein. The variant, known as EGFRvIII, is present in about a third of glioblastoma tumors. Celldex Therapeutics has licensed the vaccine and is currently enrolling patients who have tumors expressing EGFRvIII.

Even though the therapy is not quite ready for primetime, so to speak, it has been getting a good bit of attention in the news media. Dr. Sampson says he pre-(continued on page 61)
FDA Approval for Fragmin to Reduce Recurrence of Blood Clots in Cancer Patients

The FDA has approved a new indication for dalteparin (Fragmin) for the extended treatment of symptomatic venous thromboembolism (VTE) to reduce the recurrence of the problem in patients with cancer. The drug is the first low-molecular-weight heparin approved in the US for the extended treatment of recurrent VTE in patients with cancer. The condition of VTE includes deep vein thrombosis (DVT) and pulmonary embolism (PE).

“Cancer treatments and the disease itself put this patient population at significantly higher risk than non-cancer patients for developing DVT and PE,” Frederick Rickles, MD, Clinical Professor of Medicine at George Washington University Medical Center, said in a news release. The approval was based on data from the CLOT study, which evaluated the safety and efficacy of dalteparin in reducing the recurrence of DVT/PE in patients with cancer, compared with an oral anticoagulant. The CLOT study showed that, during a six-month period, nearly twice as many patients (53) treated with warfarin had at least one episode of DVT or PE compared with patients treated with once-daily dalteparin (27 patients), with most of the difference occurring during the first month of treatment. The benefit was maintained over the six-month study period. Mortality rates were similar between the study groups at the end of the study.

“The CLOT study provides clinical evidence that Fragmin is more effective than traditional oral anticoagulant therapy in reducing risk of recurrent VTE in patients with cancer,” Dr. Rickles said.

The drug had already been approved for prevention of DVT, which may lead to PE, in patients undergoing hip-replacement surgery, in at-risk patients undergoing abdominal surgery and in at-risk acutely ill patients whose mobility is severely restricted. Fragmin is also approved for prophylaxis of ischemic complications resulting from unstable angina and non-Q-wave myocardial infarction when used with aspirin.

Breaking the Complex Code of Tumor Resistance Mechanisms

Tumor resistance to cytotoxic drugs can occur at the start of therapy (primary or intrinsic resistance). As early as the first few minutes to hours after the initial period of tumor response (acquired resistance).

The mechanisms that cause intrinsic and acquired resistance are diverse. Below are some examples of the more common tumor resistance mechanisms:

**Egg box:** Responsible for transporting drugs out of the tumor cell. Efflux pumps are involved in drug concentrations. Examples are P-glycoprotein and breast cancer resistance protein (BCRP).

**Population of snipers:** Tumor cells can evade signals that normally lead to apoptosis, conferring a survival advantage by making the cell resistant to apoptotic death. An example is resistance of a surface expression of the forkhead transcription factor.

**Drug elimination:** Certain enzymes in the tumor cell play an important role in the cell’s defense against invading foreign toxins. For example, glutathione S-transferase, or GST, works synergistically with the efflux pump (MDRI) to expel drugs from the cell.

**Drug regulation:** Drugs can be trapped in specialized cellular compartments by blocking their transport out of the cell. An example is the regulation of an agent within the cytoplasmic organelles.

**Drug target alteration:** Alterations at the drug target site may impair binding. For example, variation in microtubule composition has been associated with tumor resistance.

**Drug repair:** Special enzymes within the tumor cell can identify and correct damage to the DNA that leads to genotoxicity. For example, overexpression of the enzyme ERCC1 leads to increased DNA repair of drug-induced lesions and diminished response to apoptotic signaling.

In order to overcome intrinsic and acquired resistance, new anti-cancer therapies that target mechanisms of resistance and demonstrate activity against tumors will be needed.

**Attila B-Csaba, M.D., Ph.D.,** we are currently investigating new agents that may help break the code of intrinsic and acquired tumor resistance and help physicians and patients overcome these obstacles.

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