What really makes cancer drug ‘super responders’ exceptional survival stories?

Because of incomplete reporting of cases, it’s sometimes unclear whether the patient’s exceptional survival resulted from a specific drug, a study finds

PORTLAND, Ore. – Reports of “super responders” – patients who do exceptionally well on a cancer treatment – may be driving unfounded assumptions about the effectiveness of the drugs involved, researchers caution.

“People who tell these stories should be more forthright with all relevant details and ask the toughest questions. Did the drug really do the heavy lifting?” says OHSU Knight Cancer Institute researcher Vinay Prasad, M.D., M.P.H., an assistant professor of medicine (hematology and medical oncology) in the OHSU School of Medicine.

Not every story we hear about a patient who had an exceptional response may be the result of the particular drug a patient received. It’s possible that some cases are actually patients with unusually slow-growing cancers, or disease that is broadly sensitive to many therapies, Prasad and co-author Andrae Vandross, M.D., at the University of California in Los Angeles, conclude in an article in press in the Mayo Clinic Proceedings.

The super responder phenomenon has spurred efforts at major cancer centers and the federal government to track down genetic changes in tumor DNA that predispose particular patients to respond to particular drugs that aren’t effective in most patients. The National Cancer Institute Exceptional Responders Initiative seeks to analyze as many as 300 super responses to drug therapy.

Although the strategy has been widely embraced, Prasad and Vandross noted a lack of rigorous analysis among cases already published in the biomedical literature. They reviewed 489 articles to identify 32 case reports of exceptional or super response to an anticancer drug therapy.

Incomplete reporting

The cases involved 19 tumor types, including five patients with metastatic kidney cancer, four with bladder cancer (urothelial carcinoma), and three with perivascular epithelioid cell tumors. Authors of case reports often omitted important facts, Prasad and Vandross found.

Six cases did not report the number of previous lines of treatment before the exceptional response. Among the 26 cases disclosing that information, 12 patients had received two or more previous lines of therapy.

This missing information is important because it helps doctors understand whether a patient is responding well to a particular drug, or whether a patient has
a cancer that is simply slow-growing. “People whose cancer grows slowly, or indolently, live longer and can receive more lines of therapy,” Prasad says.

The duration of response to a previous treatment was given in only 15 of the 29 cases in which patients received an earlier treatment. When reported, the response to previous treatment was often striking: seven years in one patient and more than four years in another, suggesting that perhaps some reports of super responders may not be patients uniquely sensitive to a particular drug.

In another case, a patient with an aggressive type of thyroid cancer had already lived two years before experiencing a six-month exceptional response. But given that the median survival of such patients is four months, the patient’s survival was already exceptional before starting treatment with the new drug.

Only 12 cases gave the number of similar patients treated to observe the exceptional response. Knowing this is vitally important because it puts in context the number of people who will be exposed to a potentially toxic and costly drug but receive little or no benefit so that one patient might gain.

“All reports of exceptional response should tell us how many patients had to be treated with the drug to find the person who does exceptionally well.” Prasad says. “As in many arenas of medicine, this allows us to set expectations, and help counsel patients about their chance of benefit.”

Caution warranted

Efforts to study exceptional responders are absolutely worthwhile, Prasad says. DNA sequencing can reveal rare mutations that make tumors vulnerable. And that information is likely to help future patients. But Prasad says researchers need to proceed with caution. At a minimum, he and Vandross say their study underscores the need for uniform standards of reporting of exceptional responses.

“Anecdotes are not something to be sneezed at – they can be important – but we think that when you tell the story, you should at least answer all the questions we raised in this paper,” Prasad says.

He’s also concerned that dramatic reports of super responders are spurring excess enthusiasm for off-label use of targeted drugs. “I’d be very cautious about off-the-cuff uses of these drugs,” Prasad says. “This kind of work should be done on-protocol, in a constructive research setting.”

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About the Knight Cancer Institute

The Knight Cancer Institute at Oregon Health & Science University is a pioneer in the field of precision cancer medicine. The institute’s director, Brian Druker, M.D., helped prove it was possible to shut down cells that enable cancer to grow without
harming healthy cells. This breakthrough has led to new treatments that make once-fatal forms of the disease manageable. Building on this scientific leadership, the institute is launching a large-scale research program dedicated to advancing precision early detection of lethal cancers, one of the most significant unmet needs in cancer care. The OHSU Knight Cancer Institute is the only National Cancer Institute-designated Cancer Center between Sacramento and Seattle – an honor earned only by the nation's top cancer centers. It is also headquarters for SWOG, one of the NCI's largest research cooperatives. In addition to its robust research programs, the institute offers the latest treatments and technologies as well as hundreds of clinical trials.

About OHSU

Oregon Health & Science University is a nationally prominent research university and Oregon's only public academic health center. It serves patients throughout the region with a Level 1 trauma center and nationally recognized Doernbecher Children's Hospital. OHSU operates dental, medical, nursing and pharmacy schools that rank high both in research funding and in meeting the university's social mission. OHSU's Knight Cancer Institute helped pioneer personalized medicine through a discovery that identified how to shut down cells that enable cancer to grow without harming healthy ones. OHSU Brain Institute scientists are nationally recognized for discoveries that have led to a better understanding of Alzheimer's disease and new treatments for Parkinson's disease, multiple sclerosis and stroke. OHSU's Casey Eye Institute is a global leader in ophthalmic imaging, and in clinical trials related to eye disease.