Cancer studies often lack necessary rigor to answer key questions

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Fueled in part by an inclination to speed new treatments to patients, research studies for cancer therapies tend to be smaller and less robust than for other diseases.

This raises some questions about how cancer therapies will work in practice, according to researchers at Duke Medicine, who published an analysis of nearly 9,000 oncology clinical research studies online April 29, 2013, in the journal *JAMA Internal Medicine*. The studies they looked at were registered on the ClinincalTrials.gov website from 2007-10.

The analysis is part of the Clinical Trials Transformation Initiative, a public-private partnership founded by the U.S. Food and Drug Administration and Duke University to identify and promote practices to improve clinical research.

"We need to understand the strengths and weaknesses of the clinical studies in oncology," said Bradford Hirsch, M.D., assistant professor of medicine and lead author of the study. "There are a lot of reasons for why cancer studies are different than those for other illnesses – cancer is a very grave disease and for a long time there weren't a lot of treatment options. But what we're trying to understand is if those differences justify differences in the clinical research being conducted."

Hirsch and colleagues found that oncology clinical research studies were predominantly small, early phase trials that evaluate a single treatment

without comparing it to other therapies. Larger, more rigorous trials randomly assign patients to different treatments, "blinding" both doctors and patients from knowing who received the investigational therapy in an effort to eliminate bias.

This orientation toward less robust design differs significantly from other areas of medicine. The trend is partially explained by the accelerated approval process embraced by the FDA since 1992 to improve access to treatments for life-threatening diseases such as cancer. As part of that process, early-phase clinical research studies often measure goals other than extending survival.

In addition, drugs marketed for one use and used "off label" for others have less stringent requirements for winning additional regulatory approvals.

"An inherent tension arises between the desire to use new, life-saving treatments and the imperative to develop the evidence that patients, clinicians, regulatory agencies, and advocacy groups need to make sound decisions." Hirsch said. "Unfortunately, the high prevalence of small studies that lack rigor limits the ability to assess the evidence supporting specific treatments."

Hirsch said the analysis also brought to light some disparities between the incidence and mortality of some cancer types, and the volume of clinical research being conducted. For example, lung cancer has the highest incidence, with 14.5 percent of all new diagnoses and 27.6 percent of all cancer deaths in 2010, but was the focus of only 9.2 percent of studies on the register. Meanwhile, lymphoma was the focus of 6.6 percent of studies, while it represents 4.8 percent of cancer cases and 3.8 percent of deaths.

"People who enroll in clinical trials expect their participation to lead to

future benefits for patients," said Nancy Roach, chair of the board of directors for Fight Colorectal Cancer. "Small, single-institution trials are not likely to change the standard of care. I see this paper as a call to action to encourage academic institutions to collaborate with each other on more robust trials that may ultimately lead to clinical benefit."

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