the practical aspects of the biology of childhood cancer," Parsons says.

"If we can start collecting [data] in a centralized location, then any one researcher is not going to be limited to the patients that they see at their hospital," Henderson adds. "This will enable scientists to ask very broad-reaching questions with access to biological samples where they can have good [statistical] power to answer these questions." –*Catherine Caruso* ■

Little Benefit to Breakthrough Cancer Drugs

In 2012, the FDA created the breakthrough therapy designation to speed up the development and review of drugs intended to treat serious or life-threatening diseases when preliminary clinical evidence indicates a possible substantial improvement over existing therapies. However, a recent analysis of breakthrough-designated cancer drugs indicates that although they are approved more quickly, they are no more effective, safe, or novel than drugs approved via the traditional pathway.

Because 59% of cancer medicines approved since 2014 have received that designation, researchers wanted to assess the value of these drugs, explains Jonathan Darrow, SJD, JD, MBA, of Harvard Medical School and Brigham and Women's Hospital in Boston, MA, and senior author of the study (J Clin Oncol 2018 Apr 24 [Epub ahead of print]).

Darrow and his colleagues analyzed 58 cancer drugs approved by the FDA between January 2012 and December 2017, 25 of which had received breakthrough therapy designation. The median time to FDA approval was 5.2 years for breakthrough therapies, versus 7.1 years for drugs without the designation. There was no significant difference between the two categories of drugs in median progression-free survival gains (8.6 vs. 4 months) or response rates (37% vs. 39%). Nor were breakthrough drugs more likely to have a novel mechanism of action (36% vs. 39%). Further, rates of death (6% vs. 4%) and serious adverse events (38% vs. 36%) were similar.

"The take-home message is that there's no statistically significant difference in patient benefit between the breakthrough and non-breakthrough cancer medicines," Darrow says. The findings, he adds, raise two main concerns: that patients and clinicians may have unrealistically high expectations about breakthrough therapies, and that patients and insurers are spending large amounts of money on breakthrough drugs that, in some cases, may not be any better than other available treatments (N Engl J Med 2018;378:1444–53).

In response, three physicians at the FDA penned a letter defending the program (N Engl J Med 2018;378:1457–8).

"The FDA needs the tools to identify and accelerate the approval of drugs that can substantially improve the lives of patients with serious or life-threatening diseases who have inadequate options," they wrote. "Fast-track and breakthrough-therapy designations have done just that—while not without challenges, certainly without compromising the thoroughness of our review or the standards of evidence to support approval."

They note that "not all drugs with the breakthrough-therapy designation ultimately deliver on their promise." In those cases, the designation can be withdrawn.

"All of us want really good drugs to become available to patients really quickly, and it's obviously the intention of this mechanism to make that happen," says Leonard Saltz, MD, of Memorial Sloan Kettering Cancer Center in New York, NY, who was not involved in the study. Yet he wonders if the expedited approvals of breakthrough-designated drugs result in slower approvals of other drugs. "If the goal is to identify and bring the substantially better drugs to market faster, these data would suggest that that's not being accomplished."

Saltz thinks more stringent criteria that clearly define what is required of a drug to become a breakthrough therapy could help ensure that the designation is given only to the most promising drugs.

"The concept is valid, and it's well intentioned," he says. "I think we should be objectively evaluating, 'Is it serving its intended purpose, or do we need to recalibrate?'" –*Catherine Caruso* ■

NOTED

Women with *BRCA*-mutant advanced triple-negative breast cancer are twice as likely to respond to carboplatin as docetaxel (Nat Med 2018;24:628–37). In the phase III TNT trial, women with *BRCA* gene faults who were treated with carboplatin had an objective response rate (ORR) of 68%, compared with 33% in those treated with docetaxel. This difference was not present when researchers analyzed ORR across the entire trial population.

Eli Lilly is buying ARMO Biosciences for $1.6 billion. ARMO Biosciences specializes in immuno-oncology drugs. Its leading candidate is pegilodecakin, a PEGylated form of IL10 under study in a phase III trial in pancreatic cancer, as well as earlier-stage trials in other solid tumor types, including melanoma and lung and renal cancers.

In the United States, **only 1.9% of more than 7 million current and former heavy smokers were screened for lung cancer in 2016** (J Clin Oncol 2018;36, no. 15_suppl:6504). Researchers analyzed data from the 2016 American College of Radiology's Lung Cancer Screening Registry, which tracked screening at 1,796 sites throughout the country. Screening rates were highest in the Northeast (3.5%) and lowest in the West (1%).

Men and women may have different responses to immunotherapies (Lancet Oncol 2018;19:737–46). Researchers analyzed 20 trials involving 11,351 patients with advanced cancers who were treated with immune checkpoint inhibitors. They found that although the drugs improved overall survival in both men and women, the efficacy of the drugs, on average, was significantly better in men.

President Donald Trump signed "right-to-try" legislation that allows terminally ill patients to seek experimental drugs directly from pharmaceutical companies. Previously, patients could apply to the FDA for access via a process called expanded access or compassionate use, which approved 99.5% of requests between 2009 and 2014.

For more news on cancer research, visit *Cancer Discovery* online at http://cancerdiscovery.aacrjournals.org/CDNews.