

challenging in general, not only for children's cancers," says Chesler. "To encourage commercial development, the EMA should consider creative and more robust ways of working with pharma, academia, and government to make the PIP scheme more efficient."

The FDA and the EMA already share information and communicate regularly about promising drugs, says Reaman.

"It's possible for the FDA and the EMA to require studies that may be different but complementary to increase the amount of useful information available," he says. ■

Idelalisib, Ibrutinib Show Benefits in CLL

Two recently published trials promise to transform treatment of chronic lymphocytic leukemia (CLL), researchers say, potentially ending the need for chemotherapy in this disease.

In a study published in January in *The New England Journal of Medicine*, researchers found that idelalisib (Gilead), when added to the standard treatment rituximab (Rituxan; Genentech), is more effective than rituximab alone for patients with CLL who were not considered good candidates for chemotherapy (N Engl J Med 2014;370:997-1007).

Idelalisib targets the activity of the δ isoform of PI3 kinase (PI3K). CLL cells are dependent on this PI3K isoform, but it is not expressed in most other cells, so targeting it is an effective way to attack CLL without causing debilitating side effects, says lead researcher Richard Furman, MD, director of the CLL Research Center at Weill Cornell Medical College and a hematologist/oncologist at New York-Presbyterian/Weill Cornell Medical Center, both in New York, NY.

In the trial, the drug extended progression-free survival, and improved response rates and overall survival. Researchers stopped the trial early so that patients in the control arm could start idelalisib and share the benefits.

The results were particularly striking, Furman says, because the patients had comorbidities such as kidney dysfunction or bone marrow failure, and were no longer eligible for chemotherapy.

"I never assumed we'd find an overall survival advantage," he says. "I was shocked when we saw that."

Furman was also involved in a trial published in December in *The Lancet Oncology* that showed the effectiveness of the tyrosine kinase inhibitor ibrutinib in untreated patients over age 65 (Lancet Oncol 2014;15:48-58). Ibrutinib (Imbruvica), jointly marketed by Pharmacyclics of Sunnyvale, CA, and Janssen Biotech of Raritan, NJ, targets Bruton's tyrosine kinase, which is specific to B cells.

Ibrutinib was approved by the U.S. Food and Drug Administration (FDA) on February 12 for use in patients with CLL who have received at least one previous therapy; it was approved in November 2013 to treat mantle cell lymphoma. The FDA is expected to issue a decision on idelalisib for use in CLL this spring.

Furman, who's been involved in trials of 10 different kinase inhibitors, says the approval of these two "home run" drugs suggests that the majority of CLL patients may never need chemotherapy again.

"I would not give anyone chemotherapy, period," he says.

Other researchers say that chemotherapy may still play a role in treatment, particularly in combination with a targeted therapy, in patients diagnosed in middle age or younger. Doctors don't yet know whether ibrutinib will keep CLL in check for decades, says Jennifer R. Brown, MD, PhD, director of the CLL Center at Dana-Farber Cancer Institute and an associate professor of medicine at Harvard Medical School, both in Boston, MA. That's why they may want to combine it with chemotherapy.

"In younger, fit patients who can handle chemotherapy pretty well, it might be possible to combine novel agents with chemo immunotherapy and maybe that would move us toward cure," says Brown, who is leading some combination trials for young patients now.

For his part, Furman says the publication of these two trials marks the culmination of his life's work.

"These drugs bring an end to clinical research in a lot of regards," he says. "It's a very good reason to be out of work." ■

NOTED

- **The U.S. Preventive Services Task Force recommended against using vitamin E and β -carotene supplements to reduce the risk of cancer** and cardiovascular disease because evidence suggests they offer no net benefit (Ann Intern Med 2014 Feb 25 [Epub ahead of print]). In addition, the group found adequate evidence that β -carotene supplements increase the risk for lung cancer among people at increased risk of the disease, such as smokers.
- **For the first time, the U.S. Food and Drug Administration (FDA) halted the distribution and sale of certain tobacco products currently on the market**, the authority for which was granted to the agency under the 2009 Family Smoking Prevention and Tobacco Control Act. Manufactured by Jash International, the four products—Sutra Bidis Red, Sutra Bidis Menthol, Sutra Bidis Red Cone, and Sutra Bidis Menthol Cone—were found to be not substantially equivalent to tobacco products commercially marketed as of February 15, 2007, and the company did not meet FDA requirements to continue selling them.
- **GlaxoSmithKline discontinued the manufacture and sale of Bexxar (tositumomab)**, a radio-immunotherapy with the radioactive isotope iodine-131 approved in 2003 for patients with CD20-positive relapsed or refractory non-Hodgkin lymphoma, due to relatively low profitability.
- **Astellas Pharma Inc. and Aveo Oncology terminated their agreement to develop Aveo's tivozanib for the treatment of breast and colon cancers.** In December, the companies announced that the drug was not likely to meet its primary endpoint in a phase II colon cancer trial.
- Pharmaceutical giant **Roche secured an injunction in an Indian court that prevents two companies from comparing their biosimilars to its breast cancer drug Herceptin (trastuzumab).** The court ruled that Mylan and Biocon, which developed Hertraz and CANMab, respectively, cannot refer to Herceptin or its manufacturing process, safety, effectiveness, or sales when marketing their products. Mylan and Biocon received approval from Indian drug regulators last fall to market generic versions of Herceptin.

For more news on cancer research, visit *Cancer Discovery* online at <http://CDnews.aacrjournals.org>.