was effective in patients after their cancers had become resistant to multiple TKIs or exhibited the *T3151* mutation that resistant cancers acquire.

Ponatinib produced a major cytogenetic response (MCyR) in 56% (149 out of 267) of the chronic-phase CML patients in the trial and a complete cytogenetic response in 46%. Results for accelerated- and blast-phase patients were also favorable. Pancreatitis was the most common serious side effect, but only 1 patient dropped out of the trial because of it.

Ponatinib was designed to be an especially sticky molecule that could sneak under the bulky isoleucine residue of the "gatekeeper" *T3151* mutation that keeps the other TKIs from binding to the BCR–ABL fusion protein, Cortes says.

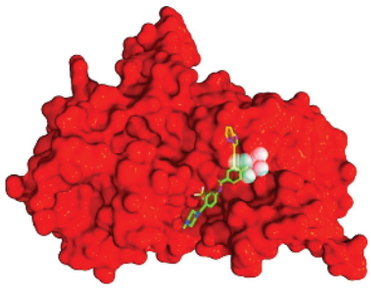
The drug produced "very deep and very rapid" responses that were not isolated to just a few groups of patients, notes Jorge E. Cortes, MD, professor of medicine at the University of Texas MD Anderson Cancer Center in Houston, who reported on PACE. "These responses happen regardless of the stage of the disease and regardless of the presence or absence of mutations."

The results presented at the ASH meeting extended findings presented at the American Society of Clinical Oncology annual meeting in June 2012 to include a full year of data from patients taking a 45-mg ponatinib pill daily.

PACE's latest results show that ponatinib has worked as planned, achieving MCyR in 70% (45 of 64) of the patients whose cancers have the *T3151* mutation. Moreover, 57% (38 of 67) of those patients with other mutations and 49% (66 of 136) with no detectable mutations also achieved MCyR.

One important question to be answered is whether ponatinib will become a first-line therapy. ARIAD Pharmaceuticals in Cambridge, MA, started a multicenter phase III trial in June that will compare ponatinib and imatinib (Gleevec; Novartis) side by side as first-line CML drugs.

In addition to imatinib, the other TKIs previously approved for CML are bosutinib (Bosulif; Pfizer), dasatinib (Sprycel; BristolMyersSquibb), and nilotinib (Tasigna; Novartis). The growing selection of TKIs means doctors can tailor treatment to patients,



ARIAD Pharmaceuticals

In a phase II trial, ponatinib produced a major cytogenetic response in 56% of patients with chronic-phase chronic myeloid leukemia.

Cortes says, drawing a comparison with the array of drugs for the treatment of hypertension from which doctors and patients can now choose. ■

Detecting Cancer by Cell-free DNA

Researchers at Johns Hopkins University have provided a proof in principle that it may be feasible to detect cancer with whole-genome sequencing technology applied to cell-free DNA found in blood samples.

The scientists took blood samples from 10 healthy people and 10 patients who had late-stage colorectal or breast cancer and sequenced circulating cell-free DNA in the blood (Sci Transl Med 2012;162:162ra154). The researchers identified structural rearrangements or copy number changes in the blood DNA of all of the cancer patients; they did not find these changes in blood DNA from healthy subjects.

"This approach is highly specific for detecting cancer," says Victor Velculescu, MD, PhD, a coauthor of the study and professor of oncology and codirector of the Cancer Biology Program at Johns Hopkins in Baltimore, MD. He says that existing blood tests for cancer depend on protein levels that can rise and fall based on events other than tumor growth, whereas the DNA changes that he and his colleagues found exist only in cancer cells. Velculescu also points out that there are many types of cancer for which researchers have yet to find a validated circulating protein marker.

Previous studies required samples of the original tumor and knowledge of the mutations in that tumor to find the same changes in blood DNA. The new technique eliminates the need for

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- **In 2012, the U.S. Food and Drug Administration approved 13 new drugs that target cancer.**
- **"Cancers claimed 8.0 million lives in 2010, 15.1% of all deaths worldwide,** with large increases [since 1990] in deaths from trachea, bronchus, and lung cancers, twice the number of deaths from the next 2 common sites for mortality (liver and stomach)," reported the researchers of the Global Burden of Disease Study 2010 (Lancet 2012;380:2095–128.)
- **Overall U.S. cancer death rates dropped by 1.8% per year for men, 1.4% for women, and 1.8% for children from 2000 to 2009,** according to the *2013 Annual Report to the Nation on the Status of Cancer*. Total cancer incidence rates declined by 0.6% per year for men, remained stable for women, and increased by 0.6% per year for children during that period.
- **President Barack Obama signed the Recalcitrant Cancer Research Act into law.** Originally known as the Pancreatic Cancer Research and Education Act, the bill mandates that the National Cancer Institute evaluate its efforts in dealing with recalcitrant cancers with certain survival rates, and focus on ways to improve outcomes.
- **Nine of 12 leukemia patients treated with infusions of chimeric antigen receptor–modified T cells responded to the therapy,** scientists in the Perelman School of Medicine at the University of Pennsylvania reported at the American Society of Hematology's annual meeting in December in Atlanta, GA. Two of the first 3 patients treated in the protocol remain healthy and in full remission more than 2 years after their treatment, the Perelman researchers reported.
- **"More than 85% of the global burden of cervical cancer occurs in developing countries, where it accounts for 13% of all female cancers,"** noted Doyin Oluwole, MD, FRCP, executive director of the Pink Ribbon Red Ribbon initiative at the George W. Bush Foundation in Dallas, TX. "Despite these staggering statistics, fewer than 5% of women are screened even once in their lifetimes."