"In the triple-negative population we're still struggling to find that subset," she said. "This study demonstrates that we can single out HER2-positive patients and look at TILs and PD-L1 expression" as potential biomarkers of response. –*Janet Colwell* ■

Rapid Responses to Avapritinib (BLU-285) in Mastocytosis

In a phase I trial, patients with advanced systemic mastocytosis, which includes mast cell leukemia, experienced rapid and durable responses, with manageable side effects, following treatment with avapritinib (BLU-285; Blueprint Medicines). Results of the trial to date were presented at the 2017 American Society of Hematology Annual Meeting in Atlanta, GA, held December 9–12.

Until recently, the standard of care for patients with advanced systemic mastocytosis has been the chemotherapeutic cladribine. In April, the FDA approved midostaurin (Rydapt; Novartis) for the treatment of the disease, and "it is catching on as the only approved targeted agent," said Daniel DeAngelo, MD, PhD, of Dana-Farber Cancer Institute in Boston, MA, who presented findings from the avapritinib trial. However, midostaurin acts broadly and lacks a high response rate, with just 17% of patients experiencing a complete or partial response.

Clearly, "there is an unmet medical need" for a more effective drug, commented Neil Shah, MD, of the University of California, San Francisco.

In comparison to midostaurin, avapritinib is a highly potent and specific oral inhibitor of mutant KIT that harbors activation loop mutants, including D816V. Approximately 90% of the 2,600 patients diagnosed with advanced systemic mastocytosis every year have this mutation, making it an attractive target.

Researchers enrolled 32 patients in a trial to assess the safety of avapritinib and determine a maximum tolerated dose. After a median treatment time of 9 months, the overall response rate was 72% among 18 evaluable patients; 56% experienced a complete or partial response. Further, 100% experienced disease control, making avapritinib "a marvelous success," DeAngelo said.

In addition to the "extremely dramatic" speed of improvement, DeAngelo said that patients demonstrated durable reductions in mast cell burden and D816V mutant allele fraction relative to baseline measurements.

The most common nonhematologic side effects of avapritinib were periorbital and peripheral edema, fatigue, nausea, abdominal pain, and diarrhea, among others. The most common hematologic adverse effects were anemia, thrombocytopenia, and neutropenia. Most adverse events were grade 1 or 2, but half of the patients experienced a grade 3 or 4 event. No patients discontinued trial participation due to these toxicities, and 30 of the original 32 patients are still continuing treatment.

Researchers tested doses ranging from 30 mg to 400 mg a day. The maximum tolerated dose wasn't reached, DeAngelo said, adding that "there didn't seem to be a dose-dependent response, but with limited numbers, it's hard to assess."

Researchers are planning to launch a phase II study in 2018 to gauge avapritinib's effectiveness in a larger number of patients with advanced systemic mastocytosis. They are also planning a phase II trial of the drug in the indolent and smoldering forms of systemic mastocytosis.

Avapritinib is also under study for the treatment of gastrointestinal stromal tumors (GIST). Avapritinib inhibits PDGFRα D842V and KIT exon 17 mutants, which play a key role in GIST.

"Other diseases can be and probably should be—and we've all recommended—tested with this agent, but it's probably limited to just a half a dozen or so KIT-driven diseases," said DeAngelo. –*Suzanne Rose* ■

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

NOTED

Prostate cancer researchers found significant disparities when they submitted identical patient samples to two different commercial liquid biopsy providers, raising the possibility that **patients could be prescribed different treatments depending upon which company performs the liquid biopsy** (JAMA Oncol 2017 Dec 14 [Epub ahead of print]). The researchers compared Guardant360 (Guardant Health), which sequenced at least part of the coding sequences of 73 genes, and PlasmaSELECT (Personal Genome Diagnostics), which analyzed coding sequences of 64 genes. Just 25 of the 40 patients in the study had at least one genetic mutation reported within the genetic sequences covered by both companies.

Jerusalem, Israel–based **Teva Pharmaceuticals announced that it will eliminate more than 25% of its workforce** over the next 2 years to reduce costs. The company is developing CT-P10[3], a biosimilar to Rituxan (rituximab; Genentech), and CT-P6[3], a biosimilar to Herceptin (trastuzumab; Genetech/Roche), and makes drugs for certain leukemias.

Cancer Research UK announced a 5-year drug-discovery collaboration between its subsidiary, Cancer Research Technology (CRT), and Celgene to discover, develop, and commercialize new anticancer treatments. The collaboration is centered on mRNA translation.

The FDA updated the label for nilotinib (Tasigna; Novartis) to include information on discontinuing the drug in patients with chronic-phase Philadelphia chromosome–positive chronic myeloid leukemia who have achieved a sustained molecular response (MR4.5) to it after at least 3 years of treatment. Criteria for monitoring patients who discontinue nilotinib are also spelled out.

The Institute for Clinical and Economic Review released its Draft Evidence Report comparing the effectiveness and value of two chimeric antigen receptor T-cell therapies—tisagenlecleucel (Kymriah; Novartis) and axicabtagene ciloleucel (Yescarta; Kite/Gilead)—for certain B-cell cancers (available at https://icer-review.org). The independent nonprofit research organization's report concludes that the therapies "provide gains in quality-adjusted and overall survival over alternative chemotherapies."

Noted

Cancer Discov 2018;8:133.