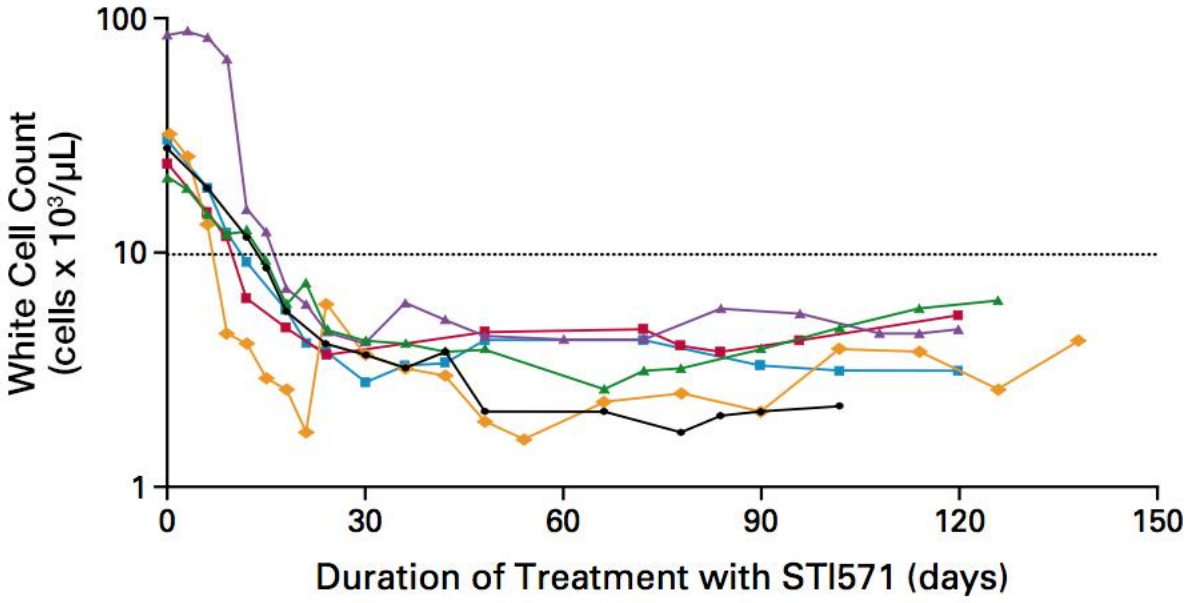

Caption: White blood cell counts in six patients with chronic myeloid leukemia treated with STI571, a drug which blocks the activity of the cancer-causing tyrosine kinase BCR-ABL. Each patient (denoted by a different colored line) received 500 mg of STI571 per day for 150 days. The dotted line represents the upper limit of the normal white blood cell count range.

BACKGROUND INFORMATION

Chronic myeloid leukemia (CML) is a cancer of white blood cells caused by a reciprocal translocation between chromosomes 9 and 22, which means that regions of these two chromosomes are swapped. The translocation brings the *ABL* gene on chromosome 9 next to a portion of the *BCR* gene on chromosome 22 to create a fusion gene called *BCR-ABL*. The *ABL* gene normally codes for a tyrosine kinase that acts as a switch to turn cell division "on" or "off." When the ABL kinase is activated, it triggers cell division by phosphorylating other proteins using ATP as a substrate. In CML patients, the fusion between *BCR* and *ABL* causes the tyrosine kinase to always be "on." This leads to uncontrolled cell division and an increase in white blood cells. Dr. Brian Druker and colleagues produced a drug called STI571 that turns off *BCR-ABL* activity by fitting into the ATP-binding site of the tyrosine kinase. Bound STI571 prevents ATP from binding, which, in turn, prevents phosphorylation of other proteins that would normally trigger cell division. To test the effectiveness of STI571, the researchers gave the drug to 83 patients with CML who had not responded to other conventional treatments. The treatment consisted of a daily drug dose, ranging from 25 to 1,000 mg for different groups of patients, while measuring the patients' white blood cell counts. The graph above shows the white blood cell counts of six patients who had received a dose of 500 mg/day of STI171.