been updated at NEJM.org. Since publication of their article, Dr. Friedman reports receiving consulting fees from Cyberonics, and Dr. Devinsky reports serving on the scientific advisory board for and owning stock in Pairnomix. No further potential conflict of interest relevant to this letter was reported.

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Abrupt Relapse of *ALK*-Positive Lymphoma after Discontinuation of Crizotinib

TO THE EDITOR: Crizotinib has been shown to have therapeutic activity in relapsed and resistant *ALK*-positive lymphomas.[1-3] Some patients receive treatment for more than 4 years without recurrence.

We describe two cases of abrupt relapse in patients with *ALK*-positive anaplastic large-cell lymphoma after discontinuation of crizotinib. Patient 1, a 26-year-old woman, began to receive therapy in June 2010. Complete remission was soon achieved, including negative results on quantitative polymerase-chain-reaction (PCR) testing to detect the nucleophosmin (NPM)-ALK messenger RNA in peripheral blood.[4] In February 2014, crizotinib was discontinued at the patient's request, with the plan to reassess NPM-ALK levels with quantitative PCR testing 1 month later. After 18 days, she presented with fever, cervical adenopathy, and dyspnea. On day 23, treatment with crizotinib was restarted at a dose of 250 mg twice daily. The fever disappeared within 24 hours, and the cervical nodes (≤3 cm) were undetectable on computed tomography (CT) on day 28. NPM-ALK positivity on quantitative PCR testing (718 copies per 10,000 copies of ABL, a value compatible with extensive disease [Fig. 1A]) decreased progressively and the NPM-ALK level returned to negative on day 78 (Fig. 1B).

Patient 2 was a 4-year-old girl who received a diagnosis of anaplastic large-cell lymphoma in May 2012. Because of the persistence of NPM-ALK positivity (114 copies) on quantitative PCR testing after four courses of chemotherapy with a partial response, crizotinib (at a dose of 280 mg per square meter of body weight per day) was initiated in August 2012, and complete remission was achieved 3 months later. Results of quantitative PCR testing became negative in October 2013 (Fig. 1B). Treatment was discontinued in October 2014. Fever and angina developed 20 days after discontinuation, followed 2 days

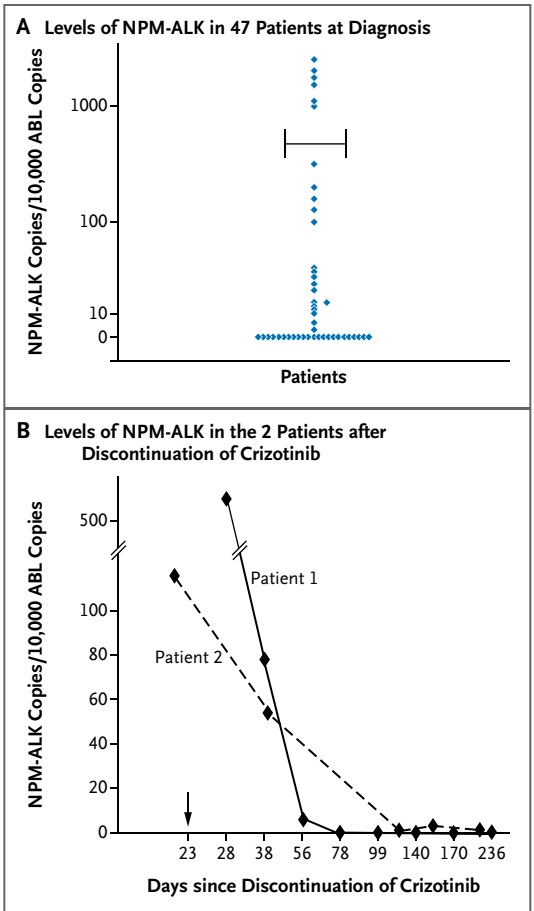

Figure 1. Detection of NPM-ALK Messenger RNA in Peripheral Blood.

Panel A shows the level of NPM-ALK measured at diagnosis by means of quantitative polymerase-chain-reaction (PCR) testing in 47 patients with *ALK*-positive anaplastic large-cell lymphoma. The bar indicates the mean (±SE) value (617±183 copies per 10,000 ABL control copies). Panel B shows the level of NPM-ALK measured by means of quantitative PCR testing after the discontinuation of crizotinib in Patients 1 and 2. The arrow indicates the reinitiation of crizotinib (in Patient 1) and the initiation of ceritinib (in Patient 2).

later by cervical adenopathy, leukocytosis (17,700 white cells per cubic millimeter, with 5% anaplastic large-cell lymphoma cells), and respiratory distress due to interstitial lung involvement. Quantitative PCR testing performed on day 20 showed 117 copies of NPM-ALK per 10,000 copies of ABL and confirmed the relapse (Fig. 1B). Treatment with ceritinib (at a dose of 450 mg per square meter) was started on day 23 and induced a rapid clinical improvement, radiologic complete remission, and negative findings on quantitative PCR testing 113 days after discontinuation of crizotinib. Both patients remained in complete remission and continued to receive treatment.

In these two patients, residual neoplastic cells persisted for up to 3 years during crizotinib treatment. Quiescent stem cells have been shown to cause persistent PCR positivity and residual disease in chronic myeloid leukemia treated with imatinib, although they do not appear to interfere with the excellent prognosis of patients with the disease.[5] These findings suggest that caution must be exercised when interrupting treatment in patients with *ALK*-positive lymphomas, since anaplastic large-cell lymphoma may recur rapidly. PCR testing to measure levels of NPM-ALK has limited ability to detect residual disease. The indicator of relapse may be the patient's clinical symptoms rather than the results of quantitative PCR testing or combined positron-emission tomography and CT.

Patients who have received crizotinib for early relapses after allogeneic bone marrow transplantation may be an exception. In these patients, temporary crizotinib treatment has resulted in durable remissions,[2] possibly because of an anti-ALK immune response mounted by the graft.

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Ebola Virus Disease among Male and Female Persons in West Africa

TO THE EDITOR: From December 2013 to August 11, 2015, a total of 20,035 confirmed and probable cases of Ebola virus disease (EVD) were reported in Guinea, Liberia, and Sierra Leone. There have been concerns that the different cultural roles or physiology of male and female persons may have resulted in the sexes being differently affected during this outbreak.[1,2]

Data on confirmed, probable, and suspected EVD cases (according to World Health Organization [WHO] case definitions[3]) were collected with the use of a standard case-investigation form[4] in Guinea, Liberia, Nigeria, and Sierra Leone. This form is completed when a case is detected and the patient is admitted to a health care facility as part of the public health response to the outbreak. We used data on confirmed and probable EVD cases in Guinea, Liberia, and Sierra Leone to compare sex-specific epidemiologic patterns. Some records were not complete, but owing to the size and overall detail of the data, we assessed whether there were any differences according to sex.

Within each district, we compared the proportion of the population who were male with the proportion of patients with EVD who were male. For each country, we also tested for sex-related differences in incubation period, time from symptom onset to hospitalization, duration of hospitalization (separately for fatalities