FDA Alert for Healthcare Professionals
Alemtuzumab (marketed as Campath)

FDA Alert [11/05]:

The Food and Drug Administration (FDA) has learned of three patients with multiple sclerosis (MS) who developed severe idiopathic thrombocytopenic purpura (ITP) while participating in a clinical study of Campath for treatment of MS. One of these individuals died from an intracranial hemorrhage. In the randomized clinical study, ITP developed approximately one to 11 months after the receipt of the last treatment with Campath. Dosing with Campath in this study is suspended at this time.

Campath is **not** approved for the treatment of MS. Campath is approved for treating B-cell chronic lymphocytic leukemia (CLL) in patients who have been treated with alkylating agents and who have failed fludarabine therapy. The Campath package insert currently includes a boxed warning about serious and rare hematologic toxicities, including autoimmune ITP, pancytopenia, marrow hypoplasia, and autoimmune hemolytic anemia associated with the use of Campath. The boxed warning also states: "**single doses of Campath greater than 30 mg or cumulative doses greater than 90 mg per week should not be administered because these doses are associated with a higher incidence of pancytopenia.**" In clinical studies of patients with CLL, autoimmune thrombocytopenia has been reported in two percent of patients with one reported fatal case of Campath-related autoimmune thrombocytopenia.

In the MS clinical study, two of the cases with ITP, including the patient who died, had received cumulative doses of Campath that exceeded the recommended cumulative weekly dosing limit in the boxed warning (see additional information about the dosing below). Both individuals had received 24 mg per day for 5 days (total dose 120 mg), followed by a second round of therapy of 24 mg per day for 3 days (total dose 72 mg) administered 12 months later. The third ITP case had received a lower dose of Campath.

This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this sheet when additional information or analyses become available.

Recommendations

As stated in the package insert (see electronic link to the approved package insert below), complete blood counts (CBC) and platelet counts should be obtained at weekly intervals during Campath therapy and more frequently if worsening anemia, neutropenia, or thrombocytopenia is observed on therapy. Campath should be discontinued in any patient with evidence of autoimmune hematologic toxicity or for severe hematologic toxicity

Data Summary

Idiopathic thrombocytopenia purpura (ITP) occurred in 3 patients with MS in the clinical study. The 3 patients are described below:

Case #1 – A patient received a 5 day course of Campath 24 mg/day, followed one year later by 24 mg/day for 3 days. Approximately 7 months after the second treatment, ataxia and ecchymoses developed, followed by obtundation and death from intracranial hemorrhage. The

platelet count had been in the normal range except for the month following the first cycle. At the time of hospital admission, the platelet count was 4000 cells/µL and antibodies to GPIIb/IIIa receptors on platelets were detected. Petechiae had been noted 1 month prior to the development of neurological symptoms.

Case #2 – A patient received Campath at a dosing schedule of 24 mg/day for 5 days, then 12 months later 24 mg/day for 3 days. Approximately 11 months following the second cycle of Campath, ecchymoses developed. Previous platelet counts had been in normal range, but on admission the count was 2000/µL, with platelet-associated IgG. After treatment with platelets, steroids, immunoglobulin and Danazol, the platelet count improved to the normal range on continued steroid treatment.

Case #3 – A patient received Campath at a dosing schedule of 12 mg/day for 5 days, then 12 and 24 months later 12 mg/day for 3 days. One month after receiving the third cycle of Campath, the platelet count was 81,000 cells/µL and the patient felt well. Petechiae subsequently developed. The platelet count at that time was 1000 cells/µL. Anti-platelet antibodies were not detected. The patient was then treated with steroids, platelet transfusion and WinRho with improvement in the platelet count.

Frequent close monitoring of hemotologic parameters is important with Campath. Patients who received Campath in the study are being monitored through the clinical trial, with close observation of hematologic parameters, and have been advised to watch for symptoms of thrombocytopenia-induced bleeding and to seek medical attention promptly if symptoms appear.