Gene therapy with LentiGlobin for sickle cell disease (bb1111, lovotibeglogene autotemcel) consists of autologous transplantation of a patient's hematopoietic stem cells transduced with the BB305 lentiviral vector that encodes the ?A-T87Q-globin gene.The phase 1-2 HGB-206 study is evaluating the efficacy and safety of LentiGlobin for sickle cell disease, and an unprespecified interim analysis of the results is now reported in the Journal.8 Here, we report a case of acute myeloid leukemia that developed in a female patient approximately 5.5 years after she had received gene therapy with LentiGlobin as part of the initial cohort (Group A) of the HGB-206 study, as well as the results of investigations to determine whether the development of acute myeloid leukemia was vector-mediated.Several somatic mutations predisposing to acute myeloid leukemia were present after diagnosis, which suggests that patients with sickle cell disease are at increased risk for hematologic malignant conditions after transplantation, most likely because of a combination of risks associated with underlying sickle cell disease, transplantation procedure, and inadequate disease control after treatment.Acute myeloid leukemia developed in a woman approximately 5.5 years after she had received LentiGlobin for sickle cell disease as part of the initial cohort (Group A) of the HGB-206 study.An analysis of peripheral-blood samples revealed that blast cells contained a BB305 lentiviral vector insertion site.