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A benefit of HLA-haploidentical bone marrow transplant with post-transplant cyclophosphamide

Although allogeneic bone marrow transplantation can cure sickle cell disease, human leukocyte antigen-matched donors are difficult to find, and the toxicities of myeloablative conditioning prior to transplants are a major risk factor for morbidity and mortality in most adults. The authors developed for patients with sickle cell disease newer bone marrow transplant regimens using nonmyeloablative conditioning regimens and human leukocyte antigen (HLA)-haploidentical donors. They conducted transplants on 17 patients who had sickle cell disease—using 14 donors with a HLA-haploidentical match and three HLA-matched related donors. The regimen consisted of antithymocyte globulin, fludarabine, cyclophosphamide, total body irradiation, and graft-versus-host disease prophylaxis with post-transplantation high-dose cyclophosphamide, mycophenolate mofetil, and tacrolimus or sirolimus. The outcomes were positive for the majority of the patients, with 10 patients asymptomatic after a median followup of 711 days and six patients entirely off immunosuppression. Only one patient developed skin-only acute graft-versus-host disease, and the disease resolved without therapy. The authors concluded that nonmyeloablative conditioning with post-transplantation cyclophosphamide resulted in low-risk complications, even with haploidentical-related donors. Therefore, full donor chimerism was not required to improve symptoms of sickle cell disease in this cohort of patients. Patients with mixed chimerism also demonstrated improvement in hemolysis, pain, and transfusion needs. The authors concluded that these findings would make it feasible to identify more donors that can provide transplants to patients with sickle cell disease. However, the authors noted that continued graft failure, at 43 percent in their study, is a concern because it remains an obstacle in haploidentical pairs.

Bolanos-Meade J, Fuchs EJ, Luznik L, et al. HLA-haploidentical bone marrow transplantation with post-transplant cyclophosphamide expands the donor pool for patients with sickle cell disease [published online ahead of print September 6, 2012]. *Blood.* doi:10.1182/blood.2012.07.438408.

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Potential infectivity of Alzheimer and Parkinson disease proteins in recipients of cadaver-derived human growth hormone

Evidence of cell-to-cell transmission of neurodegenerative disease-associated proteins prompted investigators to consider similarities to the infectious prion protein (PrP^{SC}) found in spongiform encephalopathies. Data pertaining to the potential human-to-human transmission of neurodegenerative disease-associated proteins (NDAPs) associated with non-PrP^{SC} neurodegenerative disease, such as Alz-heimer disease, are limited. The authors examined a cohort of patients who received human growth hormone (hGH) from extracted cadaveric pituitary glands (c-hGH) and explored the possible human-to-human transmission of non-PrP^{SC} NDAPs by examining the rates of neurodegenerative disease development in these patients. The authors used a data set from the U.S. National Hormone and Pituitary Program as well as the frequency of neurodegenerative diseases reported in c-hGH recipients in the published literature. The pituitary tissue from 34 autopsy patients (10 controls without neurodegenerative disease and 24 subjects with neurodegenerative disease) was also analyzed. NDAPs were identified using immunohistochemical analysis, and semi-quantitative scores of deposits of NDAPs were correlated with age at death. The investigators found a low number of pathological deposits of NDAPs in both the

neurodegenerative disease and control cases. For the national database analysis, the researchers focused on the rates of Alzheimer disease, Parkinson disease, frontotemporal lobar degeneration, and amyotrophic lateral sclerosis in patients receiving c-hGH. Sufficient data were available for 6,190 subjects, of which 796 were deceased. No cases of Alz-heimer or Parkinson disease were identified, and only three deaths due to amyotrophic lateral sclerosis were found. The investigators noted that despite the potential for infectious transmission of NDAPs, the recipients of c-hGH are not at increased risk for Alz-heimer or Parkinson disease. The few cases of amyotrophic lateral sclerosis that were identified were of unclear significance since there were no pathological deposits of ALS-associated proteins found in the human pituitary glands. Therefore, according to this study, there is no evidence that Alz-heimer disease, frontotemporal lobar degeneration-tau, or Parkinson disease-associated proteins transmit disease in humans or nonhuman primates. The authors concluded that further prospective monitoring of c-hGH recipients is required to confirm these findings.

Irwin DA, Abrams JY, Schonberger LB, et al. Evaluation of potential infectivity of Alzheimer and Parkinson disease proteins in recipients of cadaver-derived human growth hormone. *JAMA Neurol.* doi:10.1001/jamaneurol.2013.1933.

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