Treatment with GH May Be Associated with Increased Mortality

Written by Lori Alexander

Preliminary data suggest that all-cause mortality is increased among individuals who are treated with growth hormone (GH) for childhood short stature. However, causality can not be determined due to the preliminary nature of the results, as well as a low event rate, limited power, and potentially undefined confounders. The findings were reported by Jean-Claude Carel, Université Paris 7 Denis Diderot and Hôpital Robert Debré, Paris, France.

The data that were reported were from the Safety and Appropriateness of Growth Hormone Treatments in Europe (SAGhE) trial, a large study that was undertaken to evaluate the long-term health of individuals who were treated with recombinant GH in childhood in eight European countries. The study in France began 2 years before studies in other countries, and Prof. Carel reported only the preliminary mortality data from the French population-based register of children who were treated with GH.

The register included 11,035 children who were treated exclusively with recombinant GH, with treatment starting between 1985 and 1996. Of them, 6928 children and were considered to have a low mortality risk (isolated idiopathic GH deficiency, short stature in children born short for gestational age, and idiopathic short stature). The children had a mean age of 15.1 years at the end of treatment, and the mean duration of treatment was 3.9 years.

Follow-up data on vital status were available for 95% of the patients. Prof. Carel and his coinvestigators measured all-cause and cause-specific mortality and calculated standardized mortality ratios (SMRs). All-cause mortality was higher for individuals who were treated in childhood than expected in the general population (SMR, 1.33; Table 1).

Table 1. All-Cause and Cause-Specific Mortality Associated with GH Treatment.

	Standardized Mortality Ratio (95% CI)
All-cause mortality	1.33 (1.08–1.64)
Malignant neoplasms of bone and articular cartilage	5.00 (1.01–14.61)
Diseases of circulatory system	3.07 (1.40–5.83)
Cerebrovascular diseases (subarachnoid or intracerebral hemorrhage)	6.66 (1.79–17.05)

In the multivariate analysis, adjusted for height at the start of treatment, the use of a high dose (>50 µg/kg/day) was associated with a mortality rate nearly 3 times that for a low dose (<20 µg/kg/day; SMR, 2.94; 95% CI, 1.22 to 7.07).

Analysis of cause-specific mortality among individuals who were treated in childhood demonstrated increased SMRs for malignant neoplasms of bone and articular cartilage (SMR, 5.00) and diseases of the circulatory system (SMR, 3.07; Table 1). Within diseases of the circulatory system, the mortality rate for cerebrovascular diseases (subarachnoid or intracerebral hemorrhage) was more than 6 times higher than the expected rate (SMR 6.66).

In closing, Prof. Carel emphasized that the results should be interpreted with caution because of the low event rate, the statistical limitations, the lack of mortality data from the other European studies that participated in SAGhE, and the lack of morbidity data from the French SAGhE study. He added that the results highlight the need for additional studies of long-term mortality and morbidity after GH treatment in childhood.

Transitioning to Denosumab from Continuous Alendronate Therapy Further Improves BMD in Postmenopausal Women with Osteoporosis

Written by Rita Buckley

Henry G. Bone, MD, Michigan Bone and Mineral Clinic, Grosse Pointe, Michigan, USA, presented findings on the efficacy and safety of a shift from alendronate (ALN) to denosumab (DMAb) in a subset of women from the 1-year Study of Transitioning from Alendronate to Denosumab (STAND; NCT00377819) trial who transitioned to DMAb after 5 or more years of continuous ALN therapy.

STAND was a multicenter, international, randomized, double-blind, double-dummy study in 504 postmenopausal women aged ≥55 years with a bone mineral density (BMD) score of ≤–2.0 and ≥–4.0 or more who had been receiving ALN therapy for at least 6 months. Subjects were randomly assigned to either continued weekly ALN treatment or subcutaneous denosumab 60 mg every 6 months and were followed for 12 months. The primary endpoint was noninferiority of DMAb compared with ALN [Kendler DL. *J Bone Min Res* 2010].

At Month 12, total hip BMD increased by 1.9% in the DMAb group versus 1.05% in the ALN group (p<0.0001).