

**Risk of Second Neoplasms (SN) in Survivors of Childhood Cancer
Treated with Growth Hormone (GH):
An Updated Report from the Childhood Cancer Survivor Study (CCSS)**

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Introduction: GH deficiency is a common endocrine disturbance that occurs in childhood cancer survivors. GH treatment improves the growth rate and final height of survivors who have developed GH deficiency. The safety of GH therapy in this population, however, is of concern due to its mitogenic and proliferative effects. In a previous report, we did not find an increase in the risk of disease recurrence in survivors treated with GH; however, GH-treated survivors did have an increased risk of developing a SN (rate ratio [RR] 3.21) ¹. In this analysis, we have assessed the risk of GH-treated survivors developing a SN after an additional 32 months of follow up. **Patients:** We studied 361 (237 males/124 females) GH-treated survivors among a total of 14,108 survivors who were enrolled in CCSS, which is a retrospective cohort of 5-yr-survivors of childhood cancer who were diagnosed from 1970-1986 and treated at 1 of 25 centers throughout North America. The median age of the GH-treated patients was 3.5 yrs at cancer diagnosis, and 11 yrs at the start of GH treatment. The original diagnoses were: brain tumors (n=172), acute leukemia (n=122), sarcoma (n=43), neuroblastoma (n=17), and other (n=7). **Results:** During the extended follow-up, 4 new SN developed (3 meningiomas; 1 thyroid carcinoma) in survivors treated with GH, for a total of 19 SN, all solid tumors. Using a multivariate, time-dependent Cox proportional hazards model, after adjusting for the covariate effects of sex, age, alkylating agent score and radiation, the RR of GH-treated survivors developing a SN, as compared to non GH-treated patients, was 2.1 (95% CI, 1.3-3.4, p<0.002). For the subset of survivors with leukemia, the RR was marginal at 2.3 (95% CI, 0.9-5.8, p = 0.07). The RR of developing SN in brain tumor survivors treated with GH was not significant in comparison to non-GH treated brain tumor survivors (RR 1.42 [95% CI, 0.67-3.02], p=0.35). Meningiomas were the most common SN (n=9) among the GH-treated group; for survivors treated with GH, the RR of developing a meningioma was 2.6 (95% CI, 1.1-5.9, p=0.01) compared to survivors not treated with GH. **Conclusion:** Although cancer survivors treated with GH appear to have an increased risk of developing SN, particularly meningiomas, compared to survivors not so treated, the risk appears to diminish with increasing length of follow up. Continued surveillance is essential.

References: 1. Sklar CA, Mertens AC, Mitby P, Occhiogrosso G, Qin J, Heller G, Yasui Y, Robison LL. Risk of disease recurrence and second neoplasms in survivors of childhood cancer treated with growth hormone: a report from the Childhood Cancer Survivor Study. *J Clin Endocrinol Metab.* 87:3136-41, 2002.

Financial Support: NIH Grant U24-CA-55727 and the Genentech Foundation for Growth and Development.