Long-term Outcomes Among Survivors of Childhood Central Nervous System Tumors: A Report From the Childhood Cancer Survivor Study

Gregory T. Armstrong, MD, MSCE1, Kirsten K. Ness, PhD1, John Whitton2, Wendy Leisenring PhD2, Qi Liu1, Yutaka Yasui, PhD3, Lonnie Zeltzer4, MD, Sarah S. Donaldson, MD5, Melissa Hudson, MD, Leslie L. Robison, PhD1, Roger Packer6, MD

1St. Jude Children's Research Hospital, Memphis, TN; 2Fred Hutchison Cancer Research Center, Seattle, WA; 3University of Alberta, Edmonton, AB Canada; David Geffen School of Medicine at UCLA, Los Angeles, California CA; 5Stanford University School of Medicine, Stanford CA; 6Children’s National Medical Center, Washington, D.C.

Corresponding Author: Gregory T. Armstrong, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 332 N. Lauderdale Street, Mail Stop 735, Memphis, TN; Phone: 901-495-5892, Fax: 901-495-5845, Email: greg.armstrong@stjude.org

ABSTRACT

Purpose
To improve survival in childhood CNS tumors aggressive surgical intervention, radiotherapy, and chemotherapy have been employed. Long-term survivors are at risk for a broad array of late-effects secondary to tumor location and/or therapeutic interventions.

Patients and Methods
Analysis included 1,538 5-yr survivors of childhood CNS tumors (including 1,035 with Astrocytoma [AST], 306 Medulloblastoma/PNET [M/PNET], 115 Ependymoma [EP], and 82 Others). Patients, diagnosed 1970-86, had a median follow-up of 22.1 yrs (range 16.1-34.6). Outcomes of mortality, second malignant neoplasm (SMN), health status, education, employment, insurance, and marital status were assessed to determine risk associated with tumor type and treatment modality including region-specific cumulative radiation (RT) dose to the CNS.

Results
307 deaths >5 yrs after diagnosis resulted in a cumulative late mortality rate of 18.2% (95% confidence interval [CI] 16.1-20.3) at 25 yrs (EP 23.3%; M/PNET 19.0%; AST 17.3%). Standardized mortality ratios were 13.5 (95% CI 9.2-19.1) for EP; 13.1 (95% CI 10.2-16.6) for M/PNET; and 9.8 (95% CI 8.5-11.3) for AST. Late disease recurrence (n=188) and SMN (n=37) represented the most common causes of death. Cumulative incidence of SMN was 2.7% (95% CI 1.9-3.4) at 20 yrs. RT was associated with a two-fold risk of SMN (odds ratio [OR]=2.0, 95% CI 0.95-4.3). Adverse health status was reported by 57%. Treatment with RT or chemotherapy (vs Surgery only) was associated with an increased risk of severe impairment in general health (OR=2.8, p<0.001), functional status (OR=2.2, p<0.001), and activity level (OR=2.1, p<0.001). Exposure of >30Gy to any CNS region was associated with statistically significant (P<0.01) lower rates for educational attainment, marriage, employment, and personal income while exposure to <30Gy resulted in similar rates to non-irradiated patients for all outcomes.

Conclusion
Survivors of childhood CNS experience substantial long-term adverse effects of therapy and are a high priority group for intervention strategies.