Survival in Patients with Glioblastoma Receiving Valganciclovir

TO THE EDITOR: Cytomegalovirus (CMV) DNA and proteins are expressed in several types of human cancers and metastases but not in healthy surrounding tissues, suggesting a possible role for the virus in the cancer. The malignant brain tumor glioblastoma has a dismal prognosis, with a median overall survival of 12 to 14 months and a 2-year survival of 15 to 26%. We examined more than 250 cases of glioblastoma (Fig. S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Of these patients, only 1 was CMV-negative. Of the 75 patients we evaluated, the median rate of overall survival was 33 months in those with low-grade CMV infection and 13 months in those with high-grade CMV infection (P=0.04); the median rates of 2-year survival were 63.6% and 17.2%, respectively (P=0.003), which suggests that CMV affects tumor progression.

In an animal model, anti-CMV treatment reduced the growth of medulloblastoma by 72%. In the Valcyte Treatment of Glioblastoma Patients in Sweden (VIGAS) study, a double-blind clinical trial of valganciclovir involving 42 patients with glioblastoma, we found that tumor growth (the primary end point) was not significantly reduced at 3 and 6 months after surgery. However, in exploratory analyses, 22 patients receiving at least 6 months of antiviral therapy, as compared with contemporary controls, had an increased rate of 2-year survival (50% vs. 20.6%, P=0.001) and increased median overall survival (24.1 vs. 13.7 months, P=0.003). The ethics committee approved the experimental treatment protocol for patients enrolled in the VIGAS study. Owing to the promising results of this study, 28 patients at our hospital have received anti-CMV therapy for compassionate use in addition to their standard therapy (Section S2 in the Supplementary Appendix). Patients in the VIGAS study and those who were treated for compassionate use provided written informed consent for analyses of biologic samples and outcomes. Approval by the institutional review board was not required.

Here we present current retrospective data on 50 patients with glioblastoma who received valganciclovir as an add-on to standard therapy at Karolinska University Hospital as adjuvant treatment (Section S2 in the Supplementary Appendix). The rate of survival of treated patients was remarkably high: at 2 years, 62% were alive, as compared with 18% of contemporary controls with a similar disease stage, surgical-resection grade, and baseline treatment (P<0.001) (Fig. 1A, and Table S1 in the Supplementary Appendix). The median overall survival was 25.0 months, as compared with 13.5 months in the controls (P<0.001). The median survival was higher among 40 patients who received at least 6 months of valganciclovir; their 2-year rate of survival was 70%.

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Continuous treatment with valganciclovir (Panel C). The survival rate was highest among 25 patients who received continuous valganciclovir treatment after the first 6 months, with a 2-year survival rate of 90% and median overall survival of 56.4 months (P<0.001) (Fig. 1C). It is unlikely that any bias in patient selection could have resulted in these high rates of survival. Our results highlight the need for a randomized trial targeting CMV in patients with glioblastomas.

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