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Display Settings: Abstract

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Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial.

Stupp R, Hegi ME, Mason WP, van den Bent MJ, Taphoorn MJ, Janzer RC, Ludwin SK, Allgeier A, Fisher B, Belanger K, Hau P, Brandes AA, Gijtenbeek J, Marosi C, Vecht CJ, Mokhtari K, Wesseling P, Villa S, Eisenhauer E, Gorlia T, Weller M, Lacombe D, Cairncross JG, Mirimanoff RO; European Organisation for Research and Treatment of Cancer Brain Tumour and Radiation Oncology Groups; National Cancer Institute of Canada Clinical Trials Group.

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Abstract

BACKGROUND: In 2004, a randomised phase III trial by the European Organisation for Research and Treatment of Cancer (EORTC) and National Cancer Institute of Canada Clinical Trials Group (NCIC) reported improved median and 2-year survival for patients with glioblastoma treated with concomitant and adjuvant temozolomide and radiotherapy. We report the final results with a median follow-up of more than 5 years.

METHODS: Adult patients with newly diagnosed glioblastoma were randomly assigned to receive either standard radiotherapy or identical radiotherapy with concomitant temozolomide followed by up to six cycles of adjuvant temozolomide. The methylation status of the methyl-guanine methyl transferase gene, MGMT, was determined retrospectively from the tumour tissue of 206 patients. The primary endpoint was overall survival. Analyses were by intention to treat. This trial is registered with Clinicaltrials.gov, number NCT00006353.

FINDINGS: Between Aug 17, 2000, and March 22, 2002, 573 patients were assigned to treatment. 278 (97%) of 286 patients in the radiotherapy alone group and 254 (89%) of 287 in the combined-treatment group died during 5 years of follow-up. Overall survival was 27.2% (95% CI 22.2-32.5) at 2 years, 16.0% (12.0-20.6) at 3 years, 12.1% (8.5-16.4) at 4 years, and 9.8% (6.4-14.0) at 5 years with temozolomide, versus 10.9% (7.6-14.8), 4.4% (2.4-7.2), 3.0% (1.4-5.7), and 1.9% (0.6-4.4) with radiotherapy alone (hazard ratio 0.6, 95% CI 0.5-0.7; p<0.0001). A benefit of combined therapy was recorded in all clinical prognostic subgroups, including patients aged 60-70 years. Methylation of the MGMT promoter was the strongest predictor for outcome and benefit from temozolomide chemotherapy.

INTERPRETATION: Benefits of adjuvant temozolomide with radiotherapy lasted throughout 5 years of follow-up. A few patients in favourable prognostic categories survive longer than 5 years. MGMT methylation status identifies patients most likely to benefit from the addition of temozolomide.

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