
Abstract:
In patients with newly diagnosed glioblastoma that harbors a nonmethylated O(6)-methylguanine-DNA methyltransferase promoter, standard temozolomide (TMZ) has, at best, limited efficacy. The GLARIUS trial thus explored bevacizumab plus irinotecan (BEV+IRI) as an alternative to TMZ. In this phase II, unblinded trial 182 patients in 22 centers were randomly assigned 2:1 to BEV (10 mg/kg every 2 weeks) during radiotherapy (RT) followed by maintenance BEV (10 mg/kg every 2 weeks) plus IRI (125 mg/m² every 2 weeks) or to daily TMZ (150–200 mg/m²/d for 5 days every 4 weeks). The primary end point was the progression-free survival rate.
in the modified intention-to-treat (ITT) population, PFS-6 was increased from 42.6% with TMZ (95% CI, 29.4% to 55.8%) to 79.3% with BEV+IRI (95% CI, 71.9% to 86.7%; P<.001). PFS was prolonged from a median of 5.99 months (95% CI, 2.7 to 7.3 months) to 9.7 months (95% CI, 8.7 to 10.8 months; P< .001). At progression, crossover BEV therapy was given to 81.8% of all patients who received any sort of second-line therapy in the TMZ arm. Overall survival (OS) was not different in the two arms: the median OS was 16.6 months (95% CI, 15.4 to 18.4 months) with BEV+IRI and was 17.5 months (95% CI, 15.1 to 20.5 months) with TMZ. The time course of quality of life (QOL) in six selected domains of the European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire (QLQ) -C30 and QLQ-BN20 (which included cognitive functioning), of the Karnofsky performance score, and of the Mini Mental State Examination score was not different between the treatment arms. BEV+IRI resulted in a superior PFS-6 rate and median PFS compared with TMZ. However, BEV+IRI did not improve OS, potentially because of the high crossover rate. BEV+IRI did not alter QOL compared with TMZ.