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Abstracts

LB-05. PHASE III TRIAL EXPLORING THE COMBINATION OF BEVACIZUMAB AND LOMUSTINE IN PATIENTS WITH FIRST RECURRENCE OF A GLIOBLASTOMA: THE EORTC 26101 TRIAL

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BACKGROUND: Phase II data from the BELOB trial indicated that the combination of bevacizumab and lomustine might produce an overall survival (OS) benefit compared with either monotherapy for patients with first progression of a glioblastoma. The primary objective of the phase III part of EORTC 26101 is to investigate whether the addition of bevacizumab to lomustine improves overall OS in patients with first progression of a glioblastoma compared to treatment with lomustine alone. METHODS: Patients with progressive disease after standard chemo-radiotherapy with temozolomide at least 3 months off the concomitant part were randomized 2:1 between lomustine 90 mg/m^2 (cap. 160 mg) mg every six weeks plus 10 mg/kg bevacizumab every two weeks and lomustine single agent 110 mg/m^2 (cap. 200 mg) every six weeks followed by best investigators choice at further progression. In the absence of hematological toxicity > grade 1 during the first cycle in the combination arms, the dose of lomustine could be escalated to 110 mg/m^2 (cap 200 mg) in the second cycle. Neuroimaging according to a standard protocol was assessed locally and centrally. RESULTS: A total of 437 (288 and 149, respectively) patients were included. Median number of treatment cycles was 1 in the lomustine arm and 3 in the combination arm. With 329 OS events (75.3%) OS was not superior in the combination therapy arm (hazard ratio (HR) 0.95 (confidence interval (CI) 0.74, 1.21), p = 0.650, analyses stratified by EORTC online randomization system), whereas locally assessed progression-free survival (PFS) was longer with the addition of bevacizumab to lomustine (HR 0.49 (CI 0.39, 0.61). Median efficacy outcomes were: OS 9.1 (8.1, 10.1) versus 8.6 (7.6, 10.4) months and PFS 4.2 (3.7, 4.3) versus 1.5 (1.5, 2.5) months in the combination arm versus the lomustine arm respectively. Toxicity was in the expected range with more events in the combination arm being also longer on treatment. Crossover to bevacizumab occurred in 35.5% of patients in the control arm; whereas 19% of patients in the combination arm continued bevacizumab at progression. CONCLUSIONS: Bevacizumab treatment in patients with progressive glioblastoma despite prolonged PFS does not confer a survival advantage. The future challenge is to identify those patients deriving benefit from that treatment.