EORTC 26101

Despite somewhat prolonged progression-free survival, treatment with lomustine plus bevacizumab did not confer a survival advantage over treatment with lomustine alone in patients with progressive glioblastoma [1)].

Imaging necrosis on MRI scans was assessed and compared to outcome measures of the European Organisation for Research and Treatment of Cancer 26101 phase III trial that compared single-agent lomustine with lomustine plus bevacizumab in patients with progressive glioblastoma.

Methods: MRI in this post hoc analysis was available for 359 patients (lomustine = 127, lomustine + bevacizumab = 232). First, imaging necrosis at baseline being formally measurable (>10 × 10 mm, given 2 slices) was assessed. At weeks 6 and 12 of treatment, it was analyzed whether this necrosis remained stable or increased >25% calculated by 2 perpendicular diameters or whether necrosis developed de novo. Univariate and multivariate associations of baseline necrosis with overall survival (OS) and progression-free survival (PFS) were tested by log-rank test. Hazard ratios (HR) with 95% confidence interval were calculated by Cox model.

Results: Imaging necrosis at baseline was detected in 191 patients (53.2%) and was associated with worse OS and PFS in univariate, but not in multivariate analysis. Baseline necrosis was predictive for OS in the lomustine-only group (HR 1.46, $p = 0.018$). At weeks 6 and 12 of treatment, increase of baseline necrosis and de novo necrosis were strongly associated with worse OS and PFS in univariate and multivariate analysis (PFS both $p < 0.001$, OS univariate $p < 0.001$, multivariate $p = 0.0046$).

Conclusion: Increase of and new development of imaging necrosis during treatment is a negative prognostic factor for patients with progressive glioblastoma. These data call for consideration of integrating the assessment of imaging necrosis as a separate item into the MRI response assessment criteria [2)]

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