A phase II, randomized, study of weekly APG101+reirradiation versus reirradiation in progressive glioblastoma.

Abstract:

Preclinical data indicate anti-invasive activity of APG101, a CD95 ligand (CD95L)-binding fusion protein, in glioblastoma. Patients (N = 91) with glioblastoma at first or second progression were randomized 1:2 between second radiotherapy (rRT; 36 Gy; five times 2 Gy per week) or rRT+APG101 (400 mg weekly i.v.). Patient characteristics [N = 84 (26 patients rRT, 58 patients rRT+APG101)] were balanced. Progression-free survival at 6 months (PFS-6) rates were 3.8% [95% confidence interval (CI), 0.1-19.6] for rRT and 20.7% (95% CI, 11.2-33.4) for rRT+APG101 (P = 0.048). Median PFS was 2.5 (95% CI, 2.3-3.8) months and 4.5 (95% CI, 3.7-5.4) months with a hazard ratio (HR) of 0.49 (95% CI, 0.27-0.88; P = 0.0162) adjusted for tumor size. Cox regression analysis adjusted for tumor size revealed a HR of 0.60 (95% CI, 0.36-1.01; P = 0.0559) for rRT+APG101 for death of any cause. Lower methylation levels at CpG2 in the CD95L promoter in the tumor conferred a stronger risk reduction (HR, 0.19; 95% CI, 0.06-0.58) for treatment with APG101, suggesting a potential biomarker.
inhibition in combination with rRT is an innovative concept with clinical efficacy. It warrants further clinical development. CD95L promoter methylation in the tumor may be developed as a biomarker.