Impact of bevacizumab administered dose on overall survival of patients with progressive glioblastoma.

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Abstract

Bevacizumab (BEV, Avastin®) produces durable objective radiological responses of 20-26 %, median response durations of 16-18 weeks, and median overall survival (mOS) of 31-40 weeks. While the use of BEV is well-established, the lack of dose-response studies in glioblastoma (GBM) patients raises the question whether current dosing practice is optimal. As a result of differing approaches to BEV dosing that ranged from the FDA approved package insert dose of 10 mg/kg every 2 weeks to 7.5 mg/kg every 3-4 weeks, among physicians within Northern California Kaiser Permanente hospitals over 4+ years, we did an IRB-approved retrospective analysis of patients seen in Northern California Kaiser Permanente facilities and treated with BEV. Between September 1, 2008 and August 31, 2013, 181 patients received BEV for tumor progression/recurrence starting 2.6 weeks after completion of chemoradiation. The integrated BEV administered dose-week (AUCBEV) for all patients had a median AUCBEV of 3.6 mg·wk/kg. Maximum likelihood analysis found patients over 65 years did worse than younger patients (p = 0.004), women lived longer (p = 0.002), and patients treated below the AUCBEV did better than those treated above the median AUCBEV (p = 0.003). mOS for BEV starting 1 month after chemoradiation was 45 versus 68 weeks (p = 0.012) and BEV starting 3 months after chemoradiation was 40 versus 74 weeks (p = 0.0085). Dosing BEV at half the standard dose for progressive/recurrent GBM was at least equivalent to or, maybe better than standard dosing. Unexplained was the observation that females had longer OS with BEV than males.

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