Angiotensin system inhibitor

Normally prescribed with the aim to lower blood pressure, angiotensin-II (Ang-II) inhibitors were reported to reduce angiogenesis and tumour growth in several tumour models including one glioma.

Treatment with Ang-II inhibitors in combination with radiotherapy (RT) and temozolomide TMZ might improve clinical outcome in GBMs. Prospective trials are needed to test this hypothesis [1)].

Further survival advantage with ASI use was observed in rGBM patients receiving low-dose bevacizumab. These data warrant prospective evaluation of adding ASI to low-dose BEV treatment in GBM patients to improve the outcome of standard therapies [2)].

Case series

2015

A series of 81 consecutive patients, homogeneously treated with RT and TMZ for a newly diagnosed, supratentorial GBM, were analysed. The objective of this retrospective study was to assess the impact of angiotensin-converting enzyme inhibitors (ACEIs) and Ang-II receptor 1 blockers (ARBs) on functional independence, progression free survival (PFS) and overall survival (OS).

Amongst the 81 GBM patients analysed, 26 were already treated for high blood pressure (seven with ACEIs and 19 with ARBs). The number of patients who remained functionally independent at 6 months after RT was higher in the group of patients treated with Ang-II inhibitors compared to the other patients (85% vs. 56%, P = 0.01). In patients treated with Ang-II inhibitors, PFS was 8.7 months (vs. 7.2 months in the other patients) and OS was 16.7 months (vs. 12.9 months). The use of Ang-II inhibitors was a significant prognostic factor for both PFS (P = 0.04) and OS (P = 0.04) in multivariate analysis.

Treatment with Ang-II inhibitors in combination with RT and TMZ might improve clinical outcome in GBMs. Prospective trials are needed to test this hypothesis [3)].

2017

Levin et al. evaluated the effect of ASIs in glioma patients receiving chemotherapy and/or bevacizumab (BEV). Using retrospective IRB-approved electronic chart review of newly diagnosed WHO grade 2-4 glioma patients from the Kaiser Permanente Tumor Registry of Northern California, they evaluated the impact of ASIs on OS by Cox proportional hazard model analysis for subgroups who received cytotoxic therapy, cytotoxic therapy with BEV, or BEV alone, as well as those with recurrent GBM (rGBM). Of the 1186 glioma patients who received chemotherapy ASI exposure improved OS (HR 0.82; 95% CI 0.71, 0.93; p = 0.003). When stratified by BEV exposure, a sub-analysis revealed further OS advantage for the BEV group (HR 0.75, 95% CI 0.62, 0.90; p = 0.002). In a second cohort of 181 rGBM patients who received BEV in varying dosages, ASI exposure conferred an OS advantage (HR 0.649; 95% CI 0.46, 0.92; p = 0.016). Moreover, patients with ASI exposure who received low-dose BEV treatment (AUCBEV < 3.6 mg wk/kg) had a significantly longer OS (median = 99 weeks; 95% CI 44.3, 205) than those without ASI (median OS = 55.6 weeks; 95% CI 37.7-73.7; p = 0.032). ASI use is associated with longer OS in glioma patients. Further survival

advantage with ASI use was observed in rGBM patients receiving low-dose bevacizumab. These data warrant prospective evaluation of adding ASI to low-dose BEV treatment in GBM patients to improve the outcome of standard therapies [4].

[1] [3]
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[2] [4]
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