CLINICAL STUDY

Results of nimotuzumab and vinorelbine, radiation and re-irradiation for diffuse pontine glioma in childhood

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Abstract Radiotherapy is the only treatment definitely indicated for diffuse pontine gliomas (DIPG). Findings on the role of EGFR signaling in the onset of childhood DIPG prompted the use of nimotuzumab, an anti-EGFR monoclonal antibody. Assuming a potential synergy with both radiotherapy and vinorelbine, a pilot phase 2 protocol was launched that combined nimotuzumab with concomitant radiation and vinorelbine. An amendment in July 2011 introduced re-irradiation at relapse. The primary endpoint for first-line treatment was objective response rate (CR ? PR ? SD) according to the RECIST. This report concerns the outcome of this strategy as a whole. Vinorelbine 20 mg/m^2 was administered weekly, with nimotuzumab 150 mg/m^2 in the first 12 weeks of treatment; radiotherapy was delivered from weeks 3 to 9, for a total dose of 54 Gy. Vinorelbine 25 mg/m^2 and nimotuzumab were given every other week thereafter until the tumor progressed or for up to 2 years. Re-irradiation consisted of 19.8 Gy, fractionated over 11 days. Baseline and latest MRIs were assessed blindly by an outside neuroradiologist. Twenty five children (mean age 7.4 years) were enrolled as of August 2009 (median follow-up 29 months). A response was observed in 24/25 patients (96 %). The nimotuzumab/vinorelbine combination was very well tolerated, with no acute side-effects. Eleven of 16 locally-relapsing patients were re-irradiated. One-year PFS and OS rates were 30± 10 % and 76± 9 %, respectively; 2-year OS was 27 ± 9 %; the median PFS and OS were 8.5 and 15 months, respectively. This strategy generated interesting results and warrants further investigation.