U. Bode,[1]
S. Buchen,[1]
M. Warmuth-Metz,[2]
T. Pietsch,[3]
F. Bach,[4]
G. Fleischhack[1]

[1]Department of Pediatric Hematology/Oncology, University of Bonn, Children's Medical Hospital, Bonn, GERMANY, [2]Department of Neuroradiology, University of Wuerzburg, Wuerzburg, GERMANY, [3]Institute of Neuropathology, University of Bonn, Bonn, GERMANY, [4]Oncoscience AG, Wedel, GERMANY.

Final report of a phase II trial of nimotuzumab in the treatment of refractory and relapsed high-grade gliomas in children and adolescents

Background

Despite multimodal therapy most children with high grade gliomas (HGG), including glioblastoma multiforme (GM), anaplastic astrocytoma (AA) and intrinsic pontine glioma (PG) have an infaust prognosis if they relapse or are refractory to the primary treatment. Recently novel therapeutic approaches are investigated in order to improve the survival of these patients while preserving a good quality of life.

Purpose

This multicentre phase II trial was designed to explore the feasibility and efficacy of the h-R3 monoclonal anti-EGFR antibody (Nimotuzumab) in the treatment of these patients.

Patients and Methods

Pediatric patients with GM, AA or PG with radiologically proven progressive disease following primary or relapse treatment and a life expectancy of less than 4 weeks were eligible to the study. The treatment consisted of an induction therapy including a weekly short infusion of 150 mg/m^2 Nimotuzumab for six weeks, and in case of non-PD a consolidation therapy of 4 infusions in a 3 week interval. The response was documented by MRI in week 8 and 21 and only clinically in rapidly progresssive disease.

Results

Between June 2004 and April 2006 47 patients aged 4 to 17 years (median 11 years) were enrolled in this study. 46 patients were evaluable for response. According to RECIST 14 out of 46 patients showed objective responses (PR n=4, SD n=10) in the MRI as the best response with a median change in the largest diameter of the index lesion of -11% (-50% to +16%). The PR/SD were seen in 2/13 patients with GM, 2/11 with AA and 10/22 with PG. Thirteen patients continued with the consolidation therapy and showed 4 PR, 3 SD and 6 PD in week 21. The median overall survival was 4.4 months (0.3-25.4 months) and was significantly better for repsonders (median 10 months) than for nonresponders (median 4.0 months). No severe side effects related to the study medication were observed.

Conclusions

These data suggest that the repeated application of Nimotuzumab is well tolerated and safe. Nimotuzumab has cytotoxic efficacy in heavily pre-treated relapsed HGG. Based on this data a phase III trial with Nimotuzumab in newly diagnosed diffuse intrinsic pontine gliomas concomittent with radiotherapy was introduced in first quarter 2006.