

New approach for the treatment of malignant brain tumors

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Initial chemotherapy alone after surgery is just as successful as initial radiation therapy for patients from whom a very malignant brain tumor (anaplastic glioma) was removed. With this treatment, the patients survive on average > 30 months without a recurrence. A study conducted by the Neurooncology Working Group of the German Cancer Society led by researchers from Heidelberg and Zürich showed that patients in primary therapy benefit to the same extent from chemotherapy alone as from radiation alone.

In addition, the Working Group headed by Professor Dr. Wolfgang Wick, Medical Director of the Department of Neurooncology at Heidelberg University Hospital and Head of the Neurooncology Unit at the DKFZ, Professor Dr. Michael Weller, Chairman of the Department of Neurology at the University Hospital Zurich, and Prof. Andreas von Deimling, Medical Director of the Department of Neuropathology at Heidelberg University Hospital and Head of the Neuropathology Unit at the DKFZ, identified a new factor that is indicative of a positive prognosis - regardless of the form of treatment. The results of the study were published in the <u>Journal of Clinical Oncology</u>.

In Germany, around 4,500 people a year develop a glioma, a malignant brain tumor. Some 5 percent of primary brain tumors are what are known as anaplastic gliomas. They respond to treatment somewhat better than most other malignant brain tumors. The mean survival time in the study was > 80 months. As the tumors can branch out widely into the surrounding tissue, they cannot be completely removed. The subsequent



therapy in the form of combined radiochemotherapy (radiation and chemotherapy) is the current standard treatment, but it is associated with a risk of long-term toxicity to healthy <u>brain tissue</u>, causing the patient to lose cognitive abilities.

Primary chemotherapy as an equivalent treatment option

Two studies recently conducted by the European Organization for Research and Treatment of Cancer (EORTC) and the Radiation Therapy Oncology Group (RTOG) have shown that combined radiochemotherapy according to current standard practice does not yield better therapy results than radiotherapy alone. The NOA (Neurooncology Working Group) study has now also proven that chemotherapy alone after surgical removal of the tumor has an equivalent result. "This additional treatment option facilitates the further development of the treatment plan in new combinations with the long-term goal of improving the survival rate," says Professor Wolfgang Wick.

Gene mutation predicts improved outcome

Depending on their tissue composition, anaplastic gliomas are classified in different sub-groups which are assumed to have different prognoses. However, in this study, the previously distinct sub-groups of oligodendroglial tumors had an identical clinical course. With the aid of extensive molecular pathology studies of extirpated tumor tissue, the researchers identified a new prognosis factor called IDH1 mutation (gene mutation of isocitrate dehydrogenase). It is indicative, irrespective of the type of tissue of the anaplastic glioma and irrespective of treatment, of a better prognosis. The researchers proved that the already known prognosis factor "MGMT promoter methylation" is not predictive for chemotherapy, but did have prognostic value for chemotherapy as



well as for radiation alone. "The results are relevant not only for clinical routine, but for current study designs of the large study networks EORTC and RTOG as well," explained Professor Wick.

More information: NOA-04 Randomized Phase III Trial of Sequential Radiochemotherapy of Anaplastic Glioma With Procarbazine, Lomustine, and Vincristine or Temozolomide. Wolfgang Wick, Christian Hartmann, Corinna Engel, Mandy Stoffels, Jörg Felsberg, Florian Stockhammer, Michael C. Sabel, Susanne Koeppen, Ralf Ketter, Richard Meyermann, Marion Rapp, Christof Meisner, Rolf D. Kortmann, Torsten Pietsch, Otmar D. Wiestler, Ulrike Ernemann, Michael Bamberg, Guido Reifenberger, Andreas von Deimling, and Michael Weller. *Journal of Clinical Oncology*, in press.

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