Epidermal growth factor receptor targeting and its role for individualisation in radiation oncology

Mechthild Krause *

Dept. of Radiation Oncology and OncoRay National Center for Radiation Research in Oncology, Medical Faculty and University Hospital C.G. Carus, Technische Universität, Dresden, Germany
German Cancer Consortium (DKTK), Dresden, Germany
German Cancer Research Center (DKFZ), Heidelberg, Germany
Helmholtz Center Dresden-Rossendorf, Germany

Because of its over-expression in many human tumours and its association with a poor prognosis, the epidermal growth factor receptor (EGFR) is used as a therapeutic target in clinical routine and in clinical trials. Two major classes of inhibitors are used: anti-EGFR antibodies and EGFR tyrosine kinase inhibitors (TKIs). On simultaneous application of the anti-EGFR antibody cetuximab with radiotherapy in head and neck squamous-cell carcinoma (HNSCC) patients, an improvement in locoregional tumour control and survival has been shown as compared with radiotherapy alone, leading to the approval of this drug as the first molecular targeted agent in a curative radio-oncological setting. However, so far there is no hint of a superiority of this combination over simultaneous cisplatin-based radiochemotherapy; thus, both treatments are used today as alternative schedules.

While it is evident from preclinical as well as from clinical data that a major heterogeneity exists among the responses of individual patients to the combined treatment, apart from skin reactions under cetuximab treatment, there is so far no validated biomarker predicting response to cetuximab-based combined treatment, nor to cisplatin-based radiochemotherapy. Establishing predictive biomarkers would highly increase efficacy of the treatment due to the positive selection of patients. Some conclusions can currently be drawn from translationally oriented studies: at least for HNSCCs (others have not been well investigated), cetuximab application during radiotherapy improves locoregional tumour control in many but not all individual tumours, with individually impressive responses. For EGFR–TKI all local tumour control studies have been negative so far, whereas palliative effects have been shown in most HNSCCs. A promising candidate biomarker for the effect of combined radiotherapy and cetuximab in HNSCC is genetic EGFR over-expression measured by the fluorescence *in situ* hybridization (FISH) test. This marker has to be further validated in clinical settings, as well as for other tumour entities or combination schedules. Because of interactions between the treatment modalities, such biomarkers can be different between single-modality and combined-modality treatments.

Conflict of interest statement

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FURTHER READING

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* Address: Universitätsklinikum Carl Gustav Carus, Dept. of Radiation Oncology, Fetscherstr. 74, DE-01307 Dresden, Germany. Tel.: +49 (0) 351 458 5292.
E-mail address: Mechthild.Krause@uniklinikum-dresden.
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