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Imaging biomarkers during systemic therapy of cancer patients

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Metabolic imaging and early response assessment by PET are gaining importance in guiding treatment of localised and metastatic cancer [Weber JNM 2009]. Consistent results have been obtained during neoadjuvant treatment of adenocarcinoma of the oesophagus and the oesophago-gastric junction. It was demonstrated that FDG-PET is highly accurate for identifying non-responding and responding tumours within 2 weeks after the initiation of neoadjuvant chemotherapy when a quantitative threshold for metabolic response is used [Weber WA et al. JCO 2001; Ott K et al. JCO 2006]. In consecutive phase II studies we quantified the metabolic activity, defined by the standardised uptake (SUV) of 18-FDG before and during chemotherapy. We observed that after only two weeks of induction chemotherapy significant decreases of the SUV occurred. A drop of > 35% measured 2 weeks after the start of chemotherapy revealed to be the most accurate cut-off value for prediction of clinical and histopathological response after a full-course of preoperative chemotherapy lasting for 12 weeks. We have further noticed that the metabolic response to induction chemotherapy is an independent and important prognostic factor in cases of locally advanced adenocarcinoma of the oesophago-gastric junction. This suggests that PET can be used to tailor treatment according to the chemosensitivity of tumours located at the oesophago-gastric junction. The concept has been realised in the MUNICON-1 trial [Lordick F et al. Lancet Oncol 2007]. This trial prospectively confirmed that responders to induction chemotherapy can be identified by early metabolic imaging using FDG-PET. Continued neoadjuvant chemotherapy in the responding population resulted in a favourable outcome: After a follow-up 28 months the median overall survival was not reached in metabolic responders as compared to 26 months in metabolical non-responders. In metabolic non-responders, chemotherapy could be discontinued at an early stage, thereby saving time, and reducing side-effects and costs. Compared to previous studies one can deduce that the outcome of metabolic non-responders was at least not compromised by the early discontinuation of chemotherapy.

Based on these results, integration of FDG-PET can be recommended for further clinical studies in oesophago-gastric cancer but also in other tumour entitites. Important questions need to be addressed: Is the pre-therapeutic FDG uptake a relevant prognostic or predictive factor or both? Does metabolic non-response to induction treatment stand for an unchangeably unfavourable outcome or will treatment modifications lead to improved response and outcome? Another question is whether patients with metabolic non-response to chemotherapy benefit from surgery: At this stage we feel that surgery offers a considerable amount of local control, at the least, and is therefore justified as a useful treatment with calculable risks. However, non-surgical local treatment, like chemoradiation, may offer the same magnitude of local control and clinical benefit in metabolic non-responders. These questions should be addressed in future randomised trials.

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