PG 7.03 SPEAKER ABSTRACT

Optimizing neoadjuvant chemotherapy through the use of early response evaluation (PET)

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Metabolic imaging and early response assessment by positron emission tomography (PET) are gaining importance in guiding neoadjuvant treatment of localized esophago-gastric cancers. The most consistent and validated results have been obtained during neoadjuvant treatment of adenocarcinoma of the esophago-gastric junction (AEG). It was demonstrated that PET is highly accurate for identifying non-responding tumors 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 the metabolic activity, defined by the standardized uptake (SUV) of 18-FDG before and during chemotherapy, was measured. Significant decreases of the SUV after only two weeks of induction chemotherapy were observed. A drop of >35% 2 weeks after the start of chemotherapy revealed as an accurate cut-off value to predict response after a 12 weeks course of preoperative chemotherapy. It was further noticed that the metabolic response to induction chemotherapy revealed as an independent and important prognostic factor in locally advanced AEG. This suggests that PET can be used to tailor treatment according to the chemosensitivity of tumours. The concept was realized in the MUNICON-1 and -2 trials [Lordick F et al. Lancet Oncol 2007, Lordick et al. ASCO-GI 2011]. These trials 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: MUNICON-1 showed that chemotherapy can be discontinued at an early stage in metabolic non-responders, thereby saving time and reducing side-effects and costs. Compared to previous studies one could delineate that the outcome of metabolic non-responders was at least not compromised by the early discontinuation of chemotherapy. MUNICON-2 showed that the addition of neoadjuvant radiation therapy in metabolic non-responders does not lead to an evident improvement of the poor prognosis, thus showing that early metabolic non-response indicates a dismal tumor biology.

Reference(s)

Lordick F, Ott K, Krause BJ, et al. PET to assess early metabolic response and to guide treatment of adenocarcinoma of the oesophagogastric junction: the MUNICON phase II trial. Lancet Oncol. 2007;9:797–805.

Ott K, Weber WA, Lordick F, et al. Metabolic imaging predicts response, survival, and recurrence in adenocarcinomas of the esophagogastric junction. J Clin Oncol. 2006;24:4692−8.

Weber WA, Ott K, Becker K, et al. Prediction of response to preoperative chemotherapy in adenocarcinomas of the esophagogastric junction by metabolic imaging. J Clin Oncol. 2001;19:3058−65. 11408502.

PG 7.04 SPEAKER ABSTRACT

When is neoadjuvant radiochemotherapy the treatment of choice?

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The incidence of esophageal and esophageal–gastric junction tumors is rapidly increasing not only due to ageing of the population but also due to an increase of the incidence of adenocarcinomas in the last decades. For patients with resectable tumors a surgical resection is generally the treatment of choice. However, despite careful staging and patient selection the prognosis of these patients after a surgical resection is poor and characterized by local recurrences and distant metastases. One of the reasons is that in 20% to 30% of patients an irradical resection is performed. Furthermore a resection carries a substantial risk of postoperative morbidity and mortality especially in non-specialized centers.

Preoperative chemoradiotherapy may increase the number of radical resections and therefore the prognosis of these patients. We have performed a phase III study (CROSS trial) comparing chemoradiotherapy followed by surgery versus surgery alone. The preoperative chemoradiotherapy regimen consisted of weekly administrations of carboplatin targeted at an AUC of 2 and paclitaxel 50 mg/m2 q. 5 and concurrent radiotherapy 23 fractions of 1.8 Gy, 5 days per week, total doses 41.4 Gy. A total 368 patients with adenocarcinomas or squamous cell carcinomas of the esophagus and esophagogastric junction were randomized. The preoperative chemoradiotherapy regimen was well tolerated and postoperative complications and in-hospital mortality (4% in both treatment arm) were comparable. A radical resections was achieved in 92% of patients in the chemoradiotherapy arm versus 69% in the surgery alone arm. Median overall survival was 49.4 months in the preoperative chemoradiotherapy followed by surgery arm versus 24 months in the surgery arm. Overall survival was significantly better ($p = 0.003$) in the chemoradiotherapy followed by surgery arm (HR 0.657; 95% CI 0.495–0.871).

Based on this study and meta-analyses preoperative chemoradiotherapy can be considered standard of care for patients with esophageal cancer. Important questions still remain such as are the results of definitive chemoradiotherapy comparable to the results of preoperative chemoradiotherapy followed by surgery and what is the role of delayed surgery for residual disease or recurrences after definitive chemoradiotherapy?

There is also a debate whether tumors arising of the esophageal-gastric junction should be treated with preoperative chemoradiotherapy (CROSS trial) or with preoperative chemotherapy as is suggested in the MAGIC and the FNCLCC and FFCD trial. Only in the POET trial preoperative chemotherapy was compared with preoperative chemoradiotherapy and although there was a trend for improved survival in favor of the preoperative chemoradiotherapy arm the difference in survival was not significant (hazard ratio adjusted for randomization strata variables 0.67, 95% CI 0.41–1.07). These issues will be further discussed.

Friday, 23 March, 12:00−12:30

Keynote Lecture II

PG 8.01 SPEAKER ABSTRACT

Writing and submitting an outstanding scientific manuscript

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Medical journals, such as the JCO, are complex enterprises, and require the close cooperation of authors, editors, reviewers and readers. Each journal decides its own territory, and the JCO has elected to represent a multidisciplinary hematology-oncology journal, rather than focusing on a single disease site or modality. Popular journals may receive more than 3000 original reports annually, but upper level journals publish only 10−15%. Editors monitor online accesses and other sources to determine reader's interest apart from original reports, especially editorials, reviews and guidelines or consensus statements. An important metric for journals, is the speed of manuscript review and publication. To sped publication time, most journals publish papers on-line ahead of print, which is the official Medline date for CVs and other purposes. When submitting MSS, authors should read the journal's information for authors, so that standard requirements are met. A popular metric of journal success is the Impact factor, which is a mathematical mean of the number of citations for the journal's original reports for two full years, divided by the number of papers published. This means that journals with high impact papers, but few papers published will have the highest impact factors. The JCO, which published about 650 papers per years, had an impact factor most recently measured at 17.793, the highest among peer-reviewed hematology-oncology journals. Why do we publish? Because they represent accomplishment in academic medicine, primary documentation of research data, evidence of expertise through writing an authoritative review paper or book chapter and are a major determinant in achieving academic promotion and career development. There are three key steps for getting published in any journal: Do good science, write well and submit what the journal publishes. For any clinical trial report, the trial must be registered when the study begins, in any recognized database, such as ClinTrials.gov, or the paper will not be reviewed or published by recognized journal. For more information read the JCO Editorial on this topic by Haller, November 2008: "Will your paper be publishable?" In preparing a manuscript, be aware of journal guideline for potential conflicts of interest; each journal may have their own specific policies, but general guideline may be found on the ICMJE and WAME websites. The intent of these policies is not to prevent authors with these relationships from publishing their work. It is merely intended that any relationships be identified openly so the Editors and peer reviewers can make informed decisions about submitted manuscripts. It remains for readers to determine whether the authors' outside interests reflect a possible bias in the conclusions presented, and not all potential conflicts of interest are financial, including personal relationships and academic competition. To qualify as an author, each listed author must have generated at least part of the intellectual content of the paper, and should have taken part in writing and revising the intellectual content. Solely entering patients on a trial does not qualify for authorship: acknowledgements are appropriate. All authors should be able to defend publicly in the scientific community the intellectual content of the paper for which responsibility is taken. If a communications firm or company writes your draft (ghostwrites), NEVER have them communicate with the journal directly, and always use their words as a draft. Medical writers should not be listed as authors, but should be listed under "acknowledgements". When preparing a manuscript, be wary of multiple papers from same research and avoid "salami science" – slicing data too thin. Avoid the "LPU": the "Least Publishable Unit", and republish only if there is substantial new data. Don't plagiarize yourself or violate previous copyright; when in doubt, consult ICMJE and WAME guidelines. For papers submitted to clinical journals, ask yourself