CORRESPONDENCE

Pancreatic Cancer – Low Survival Rates

by Prof. Dr. med. Dr. h. c. Hans G. Beger, PD Dr. med. Bettina Rau,
PD Dr. med. Frank Gansauge, Dr. med. Gerd Leder, PD Dr. med. Michael Schwarz,
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Gemcitabine More Useful

From the point of view of the "DKG-S3 Guideline Committee for Exocrine Pancreatic Carcinoma", the following points should be discussed which were neglected in the review of Beger et al..

In the paragraph on adjuvant chemotherapy (Cx), the authors imply that the 5-fluorouracil bolus protocol, as used in the ESPAC-1 study, is the standard adjuvant chemotherapy after R0-resection. However, the S3 guideline (3) recommends that the 5-fluorouracil bolus protocol should not be used. On the contrary, the guideline unambiguously recommends adjuvant Cx with gemcitabine, because disease-free survival and overall survival were improved by gemcitabine in the CONK0-001 study (2). Even though it was expected that bolus 5-fluorouracil and gemcitabine would be equipotent in the ESPAC-III study, gemcitabine would still be preferable as Cx, as the tolerability is better and the handling simpler.

The authors' sentence "Some data, however, demonstrate that adjuvant palliative chemoradiotherapy can improve the prognosis for the R1/R2 resected patient" is likewise inconsistent with the S3 guideline.

Based on the subgroup analysis of the CONK0-001 study, this advocates additive palliative Cx with gemcitabine. Although a metaanalysis (4) found a trend towards benefit with adjuvant radiochemotherapy in comparison with resection alone, there are no data comparing this with chemotherapy alone. Because of the markedly higher toxicity and stress to the patient in comparison to gemcitabine for what is usually palliative treatment, the guideline regards this procedure as only an option for the individual patient. The guideline recommends that radiochemotherapy after R1 resection should, if at all possible, be performed in the form of randomized controlled study protocols. We are urgently awaiting the results of prospective randomized studies to clarify this important question.

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Conflict of interest statement

The author acts as an adviser to Lilly and receives honoraria for presentations.

In Reply:

It was an essential aim of the article "Pancreatic Cancer - Low Survival Rates" to describe the levels of dissemination of the carcinoma and the possibilities of surgical resection. There is no general agreement on what constitutes early pancreatic carcinoma. 30-40% of patients with advanced ductal pancreatic carcinoma exhibit infiltration of the lymph nodes in the aorto-caval compartments (1). In 35-60% of cases, the carcinoma extends into the extrapancreatic neural plexus.

The UICC protocol for the R-classification of pancreatic carcinoma provides only an inadequate description of the actual residual tumor status, based on the evaluation of four cut edges of the tumor.

After systematic evaluation of the resection borders, the frequency of R1 resection rose from 15-30% to clearly more than 50% (2).

If lymph node resection only incorporates the local lymph nodes, but not the extracorporeal neural plexus, many patients retain residual tumor distant from the resection borders, in spite of the R0 resection according to the UICC protocol. This is the reason that only 10% of patients survive 5 years after R0 resection (observed survival).

The ESPAC-I study from the "European Study Group of Pancreatic Cancer" has shown for the first time that adjuvant chemotherapy provides a survival benefit in comparison with resection. This study has a large number of cases and a high level of evidence. The 5-FU bolus protocol of the ESPAC study was explicitly not addressed and not raised to the level of the standard treatment. Gemcitabine is currently the first line chemotherapy for advanced pancreatic carcinoma. On the other hand, the median survival advantage after gemcitabine monotherapy is unsatisfyingly low at 5 to 6 months and the partial response rate has the very low value of between 5.4% and 14.3% (3).

There are prospective study results and metaanalyses on the efficacy of palliative radiochemotherapy after R1/R2 resection. Stocken's metaanalysis concluded that adjuvant radiochemotherapy has greater efficacy than chemotherapy alone after R1 resection (4). Khanna's meta-analysis has shown that adjuvant, additive radiochemotherapy gives a survival benefit of 12% after two

years (5). In the USA, palliative radiochemotherapy ("chemoradiation") has become the standard therapy after R1/R2 resection. DOI: 10.3238/arztebl.2008.0656

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Conflict of interest statement

Professor Beger is founder and chair of the German German Pancreatic Cancer Foundation, c/o Ulm University Hospital. He initiated ESPAC and as such he participated in the ESPAC I study.