

BACKGROUND INFORMATION FOR MEDICAL TRADE MEDIA

Gastric Cancer

95% of gastric cancer cases are adenocarcinomas, i. e. tumors originating in the gastric acid producing cells of the mucous membrane. Gastric cancer is the fourth most common cancer type worldwide (Globocan 2002), however, there is a high variance between different countries and regions. In most industrial countries the incidence of gastric cancer has been decreasing over the last decades and is today about half as high as it used to be 30 years ago. Generally the number of new cases diagnosed in the USA and Western Europe is significantly lower than in Asia, Eastern Europe or developing countries. In 80 % of cases the disease is diagnosed in a fairly advance state (this also applies to industrial countries) and therefore the prognosis is generally rather unfavorable. This is reflected by a comparatively high mortality rate. In men the incidence peak is at the age of 70, in women it is five years later.

First and foremost nutrition seems to play an important role in the development of gastric cancer. Apart from nutritional habits another established risk factor is the colonization of the stomach with the bacterium *Helicobacter pylori*. Genetic risk factors could not be accounted for, although first degree relatives show a higher risk of developing the disease than the average population.

Diagnosis

Gastric cancer grows without displaying any symptoms for a rather long period of time and thus is often only diagnosed by coincidence. Signs of discomfort, however, suggesting a development of the disease are manifold. They include a feeling of pressure or pain in the upper stomach region, a sudden aversion to particular food or drinks, abnormal fatigue, nausea and frequent vomiting. Advanced symptoms are dysphagia, weight loss, melena and hematemesis.

The diagnosis is confirmed by gastroscopy during which biopsy samples are taken for histological analysis. Distant metastases appear most commonly in the lungs, bones, liver, lymph nodes of the abdomen and peritoneum. They can be detected by X-ray examination of the thorax, bone imaging,

sonography, CT or MRI. In order to search the abdominal cavity for metastases a laparoscopy may also be indicated.

The patients' prognosis depends heavily upon the tumor stage. Whereas for patients in stage I the 5 year survival rate is as high as 80%, in stage IIIB it lies approximately at 20 % and is in stage IV below 5 %.

Therapy

The only curative therapy option is a partial or complete resection of the stomach (gastrectomy) and the regional lymph nodes. Depending on the general condition, the operation can be preceded by a neoadjuvant chemotherapy to reduce the size of the tumor, which in a first phase III study displayed a significant improvement in the 5 year survival rate. If the tumor has penetrated the stomach wall an extended gastrectomy can be performed in which the surrounding tissue is removed. In this case a section of the large or small intestine can be removed and connected to the esophagus and intestines to serve as a substitute stomach. The necessary digestive enzymes and vitamins have to be administered via medication.

If after the surgery tumor tissue has remained an additive chemotherapy is administered which might enable a second successful resection. In case of inoperable tumors or distant metastases, a palliative chemotherapy can be administered to alleviate the symptoms and prolong life. Current standard medication includes combinations of Epirubicin/Cisplatin/5-FU (ECF), 5-FU-Folinic acid/Cisplatin (FLP) and Mitomycin/Cisplatin/5-FU (MCF). Since early 2007 combinations with oral Fluoropyrimidin (Capecitabine) are also approved for the treatment of advanced gastric cancer. For patients with a poor general condition a mono therapy with 5-FU can be administered.

The benefit of adjuvant chemotherapy and/or radio therapy in order to reduce the risk of relapse after R0 resection has not been confirmed yet and is being studied in clinical trials. The trifunctional antibody catumaxomab could provide a more effective and tolerable alternative. catumaxomab binds to the overexpressed cell adhesion molecule EpCAM (Epithelial Cell Adhesion Molecule) which is found on gastric cancer cells. Pre-clinical data has shown that catumaxomab is also capable of recruiting T-lymphocytes and accessory cells, which via their mutual stimulation could lead to a stronger immune response against the tumor cells. In the two active phase II studies catumaxomab is being tested in patients with advanced adenocarcinoma

having a high risk of relapse but still the chance of R0 resection. In the study IP-REM-GC-02 the administration of catumaxomab following curative gastrectomy is compared to gastrectomy alone. In the second study, IP-REM-GC-03, neoadjuvant chemotherapy precedes the gastrectomy. The primary endpoints of these studies are safety and tolerability of the trifunctional antibody, secondary endpoints are efficacy parameters such as overall survival and progression free survival.

(Status: June 2007)