

With the diagnosis of pancreatic cancer, the majority of patients are faced with an unexpected tragedy. There is a persistently low rate of curability, a so-called case fatality rate of around 95%.

Complete resection is the prerequisite for curation, but only one-fifth of the patients are considered for surgical therapy. Even so, only about half of these individuals finally undergo successful, complete resection. Whereas nowadays surgery can be performed with low rates of perioperative morbidity and mortality at experienced high-volume centers, postoperative relapses are observed frequently. Neoadjuvant strategies to improve surgical resectability and the overall cure rate remain experimental, but due to the results of different trials, adjuvant treatments strategies are becoming standard worldwide. Transatlantic differences in the interpretation of study results with the use of chemoradiation probably will be overcome by the recent results of adjuvant chemotherapy in patients with adenocarcinoma of the pancreas, which have shown significant benefit in relapse-free survival, 3- and 5-year survival, and therefore—most likely—cure [1]. Ongoing studies will definitely clarify the role and kind of chemotherapy to be recommended for patients resected completely (R0) and those with microscopic involvement of the resection margin (R1).

For the majority of patients with nonresectable, locally advanced, metastasized, or relapsing pancreatic cancer, progress has been limited for several years. It took more than 10 years from the approval of gemcitabine for the treatment of advanced adenocarcinoma of the pancreas—and a great number of large-scaled phase III trials—before a second improvement in systemic therapy was implemented in patient care.

Erlotinib, a tyrosine kinase inhibitor blocking epidermal growth factor (EGF) receptor-mediated downstream signaling, succeeded in improving outcome in patients with advanced pancreatic cancer when applied in combination with gemcitabine, with a hazard ratio of 0.8 resulting in a 7% excess in 1-year survival as compared to gemcitabine plus placebo [2]. Due to this study, erlotinib obtained approval in the United States and Europe and is on the way to finding its place in routine treatment.

Confirming former nonsignificant results of gemcitabine in combination with capecitabine, it was recently demonstrated that this combination of cytotoxic drugs improved median and 1-year survival in a prospective randomized but non-placebo-controlled trial [3].

The impact of these data for standard care of patients with adenocarcinoma of the pancreas cancer needs to be defined. As adverse effects of cytotoxic drugs and targeted therapies differ, tailoring patient-specific first-line therapy has become a challenge for oncologists.

An improvement in quality of life, estimated by the clinical benefit response, occurs in a relevant proportion of patients due to first-line therapy with gemcitabine [4]. Therefore an increasing number of patients with pancreatic cancer progressing while on first-line therapy need to be considered for second-line therapy, based on their good performance status. The identification of principally active cytotoxic drugs, such as oxaliplatin (together with folinic acid and fluorouracil) or taxanes, antibodies, and small molecules, such as erlotinib and sorafenib, offer second-line treatment alternatives that have to undergo evaluation in clinical trials. Initial results favor oxaliplatin-based therapy [5, 6].

These small steps forward in the systemic therapy of pancreatic cancer give rise to some prudent optimism. In order to alter the perspectives of patients with pancreatic cancer, further understanding of the basic aspect of disease development as well as methods for screening or early diagnosis of this disease have to be developed. It is the aim of this issue of *Recent Results in Cancer Research* to compile the available knowledge concerning pancreatic cancer.

Acknowledgements

The editors recognize and acknowledge the important contributions of the various authors, all of them involved in the challenging effort of fighting this frightening cancer.

References

1. Oettle H, Post S, Neuhaus P, et al (2007) Adjuvant chemotherapy with gemcitabine versus observation in patients undergoing curative-intent resection of pancreatic cancer. A multicenter randomized controlled trial. *JAMA* 297:267–277
2. Moore MJ, Goldstein D, Hamm J, et al (2007) Erlotinib plus gemcitabine compared with gemcitabine alone in patients with advanced pancreatic cancer: a phase III trial of the National Cancer Institute of Canada Clinical Trials Group. *J Clin Oncol* 25:1960–1966
3. Cunningham D, Chau I, Stocken D, Davies C, Dunn J, Valle J, et al (2005) Phase III randomised comparison of gemcitabine (GEM) versus gemcitabine plus capecitabine (GEM-CAP) in patients with advanced pancreatic cancer. *Eur J Cancer* 3:4 [Suppl]
4. Burris HA 3rd, Moore MJ, Andersen J, et al (1997) Improvements in survival and clinical benefit with gemcitabine as first line therapy for patients with advanced pancreas cancer: a randomized trial. *J Clin Oncol* 15:2403–2413
5. Oettle H, Pelzer U, Stieler J, Hilbig A, Roll L, Schwaner I, Adler M, Detken S, Dörken B, Riess H (2005) Oxaliplatin/folinic acid/5-fluorouracil [24 h] (OFF) plus best supportive care versus best supportive care alone (BSC) in second-line therapy of gemcitabine-refractory advanced pancreatic cancer (CONKO 003). *Clin Oncol* 23:16S, abstr 4031
6. Riess H, Pelzer U, Stieler J, Schwaner I, Heil G, Görner M, Mölle M, Hilbig A, Dörken B, Oettle H (2007) A randomized second line trial in patients with gemcitabine refractory advanced pancreatic cancer—CONKO 003. *J Clin Oncol* 25:18S, abstr 4517

Pancreatic Cancer

Riess, H.; Goerke, A.; Oettle, H. (Eds.)

2008, XII, 186 p. 48 illus., 12 illus. in color., Hardcover

ISBN: 978-3-540-71266-4