Editorial: Multimodality Treatment in Pancreatic Ductal Adenocarcinoma – Current Options and the Future Impact of Molecular Biological Profiling

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Dear readers of *Visceral Medicine*, this special issue focuses on up-to-date topics of clinical management as well as on late-breaking basic research developments. It is dedicated to our former teachers and pancreatic researchers Guido Adler and Hans-Günther Beger at the University of Ulm.

Pancreatic ductal adenocarcinoma (PDAC) is still one of the most dismal malignant diseases worldwide and has to be regarded a major health problem in many developed countries. More than 90% of patients are going to die after diagnosis from this disease. Within the last 30 years, the incidence increased by 2.3-fold to about 550,000 cases annually [1]. This trend is related to a growing and aging society as well as a rising prevalence of pancreatic cancer risk factors with higher frequencies in more developed countries. Risk factors include smoking, high fasting glucose/diabetes mellitus, and obesity as well as exposure to environmental carcinogens [1]. A familiar predisposition is rare but associated with a lifetime relative risk up to 50 compared to the normal population [2].

With this knowledge, a great deal of effort has been undertaken in clinical and scientific areas to battle PDAC within the last decades. Thereby, outstanding improvements in the field of diagnosis could be established including high-quality thin, ideally sub-millimeter-sliced, multidetector computed tomography with pancreatic and portal-venous phases as the gold standard tool for cross-section imaging [1]. In addition, endoscopic ultrasound has been specially optimized to obtain diagnostic material via fine needle aspiration or core needle biopsy [1]. It is meanwhile also established to report imaging findings within a well-structured report. This diagnostic classification may allow an individual and more precise

prediction of surgical resectability, which can be basically divided in resectable, borderline-resectable, and non-resectable [1]. Meanwhile, several neoadjuvant strategies with chemotherapy as backbone have been established for borderline- and locally non-resectable cases in many countries. This may enable borderline-resectable cases a better chance for an R0-resection in the future and to convert locally non-resectable cases to potentially resectable ones [3].

Surgical resection of PDAC remains the mainstay of potential cure. Within the last 4 decades of pancreatic surgery, many technical inventions improved the quality and safety, and the outcome [1]. Pancreatic resections can be performed in a relatively limited time without significant blood loss also including venous reconstruction without problems in specialized centers. Interdisciplinary perioperative management in parallel improved as well. In addition, performance status and tumor marker level (CA19-9) are included into the decision making besides sole technical resectability. These means can help to further reduce perioperative morbidity and mortality as well as the risk of early postoperative recurrence [1]. Besides, minimal-invasive approaches especially for left-sided tumors become more and more established also as standard approach for oncologic procedures. With this regard, robotic surgery has opened up new degrees of freedom compared to laparoscopic surgery with regard to detailed intraoperative imaging and visualization, ability of lymph node dissection, and tumor resection, as well as of minimal-invasive total reconstruction. Despite these advances pancreatic fistula with its concomitant severe problem of postoperative pancreatic hemorrhage remains a difficult and sometimes unsolvable problem.

Therefore, in-hospital mortality presently remains about 5% even in specialized centers [1].

Adjuvant and additive treatment of PDAC after tumor resection is well established. It is going to be more and more optimized by tumor-tailored approaches, and can further increase cure rates for some patients [1]. For most patients with locally irresectable and distant disease palliative systemic treatment is performed. Although statistically significant clinical effects are detectable, these are presently of minor relevance compared to palliative treatment of other malignant diseases.

Basic research has been challenging pancreatic cancer for multiple decades. Despite having increased the understanding of its pathology, no curative approach could be developed so far. Research has focused on early detection, prediction of disease development, and medical treatment [1]. Modern individual tumor drug sensitivity testing includes refined techniques like liquid biopsy or organoid cultures [4]. These modeling systems address an increasing amount of the cancer's features like tissue environment crosstalk but are still far from being routine [4].

Under the bottom line, many improvements due to basic, translational, and clinical research involving PDAC have been achieved [1]. Disappointingly, deaths from PDAC have increased to the same extent as the incidence in the last 30 years, namely by 2.3-fold [5]. Although PDAC only ranks 9th and 10th (females and males) among cancer incidence in the USA, it meanwhile ranks 4th for both sexes among cancer-related mortality [1]. It is furthermore projected that by 2030, PDAC will have overtaken colorectal, prostate, and breast cancer to move up to second place in cancer related mortalities [6]. Therefore, it seems mandatory to rapidly transfer recent scientific findings into the standard clinical management re-

sulting in more and more individualized treatment pathways and precision medicine. Within "The Know Your Tumor" program, personalized tumor profiling with targeting actionable mutations demonstrated a benefit for those patients receiving matched therapies [7].

Therefore, to spark further improvements, the aim of this special issue of *Visceral Medicine* is to provide the reader with a condensed up-to-date collection of reviews of three highly interesting preclinical basic research areas in combination with three state-of-the-art reviews covering core topics of surgical and oncological treatment focusing on individualization. Patil et al. [8] perfectly summarize the cell type of PDAC origin with possible implications for prognosis, while Versemann et al. [9] and Long et al. [10] point to potentially new treatment strategies involving epigenetic changes and exosomes, respectively. Up-to-date multimodal treatment options are displayed by Ettrich et al. [11], while Mota Reyes et al. [12] and Nienhüser et al. [13] give overviews of individualized surgical strategies in primary and recurrent cancer, respectively.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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