UNITED EUROPEAN GASTROENTEROLOGY

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UEG Position Paper

Bringing pancreatic cancer treatment to the 21st century: detect and treat the disease earlier and better

Key figures

Pancreatic cancer is aggregating dramatic figures in terms of number of cases, survival rates, and forecasts for incidence and survival in upcoming years. There has been little improvement in patient outcomes over the last four decades:

- Pancreatic cancer is currently the fourth biggest cancer killer and the eight most common cancer in both sexes, predicted to be the second biggest killer by 2030.
- Across Europe, the number of deaths from pancreatic cancer has almost doubled in the past three decades and it now claims the lives of over 132,134 EU citizens in 2020. Forecasts predict that the number of cases and deaths will both increase by 40% by 2035.
- Pancreatic cancer has still the lowest survival rate of all common cancers, with life expectancy of just a few months at the time of diagnosis at an advanced stage. This highlights the extremely poor outlook for patients.

UEG's main messages

Considering these figures, this position papers calls for policy makers to urgently address the following research gaps:

1. Enhance our understanding of this complex disease to improve primary prevention
2. Identify the correct tools to achieve earlier diagnosis
3. Develop new strategies to overcome therapy resistance
4. Improve the quality of life and patients' experience and reported outcomes

Research gaps to address now to defeat pancreatic cancer

1. Enhance understanding of this complex disease

Pancreatic cancer is a genetically extremely heterogenous disease, characterized by an abundant stroma reaction and a highly immune-evasive phenotype, contributing to the frequent resistance to systemic therapies observed in this tumour. Moreover, most tumours arise from macroscopically invisible precursor lesions, making early diagnosis difficult with most patients being diagnosed at an advanced, unresectable stage.

The way forward:

- Identify novel drivers of tumour development including genetic drivers and inflammatory cues such as obesity- and diabetes-induced or microbiome-associated modifiers in order to establish novel diagnostic, prognostic and predictive biomarkers.

- Improve the understanding of complex tumour biology and decipher events driving tumour development and therapy resistance through joint efforts using state-of-the art -omics and non-omics technologies.
- Understand the key signalling nodes enhancing tumour development, progression and therapy resistance will foster the development of novel precision medicine avenues based on molecular signatures.

2. Correct tools for earlier diagnosis

Although certain genetic mutations and risk factors have been detected, only about 2% of pancreatic cancer cases are explained by inherited mutations. The heterogeneity of the disease, the absence of clear-cut risk constellations and detectable preneoplastic stages in most cases, and the difficult-to-reach anatomic location makes screening for early diagnosis a significant challenge.

The way forward:

- Develop new methods to better define persons-at-risk and identify algorithms for screening in the general population.

- Develop novel imaging technologies to detect precancerous lesions or tumours at a very early stage, with joint technology development efforts by industry and academic partners.

- Identify biomarkers suitable for reliable detection of preneoplastic lesions or early tumours in liquid biopsies.

- Find the tools for a safe, relevant, non-invasive and specific screening of precancerous lesions in population.

3. Strategies to overcome resistance to systemic therapies

Only 20% of pancreatic cancers are resectable upon diagnosis. Even after curative resection, many patients succumb due to later local or metastatic recurrence. In an advanced stage, pancreatic cancer is characterized by a high rate of resistance to current chemotherapies and targeted treatment options.

The way forward:

- Develop molecular treatment approaches targeting both tumour cells and components of the surrounding microenvironment by the characterization of the distinct subtypes and the heterogeneity of pancreatic cancer.

- Implement Europe-wide umbrella trial platforms.

- Explore optimal combinations or sequence of chemotherapies, targeted, radiotherapeutic and immunomodulating modules for metastatic tumours.

- Define multimodal approaches and treatment sequences for resectable and locally advanced tumours in order to minimize the risk of systemic spread and to maximize the chances for complete surgical resection, to improve long-term survival.

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4. **Instruments to measure the quality of care and patients' reported outcomes**

Although there is increasing evidence that patients' engagement is associated with improved clinical outcomes, in the field of pancreatic cancer, there are limited data on patients' experience measures, patients' reported outcomes and on the role of caregivers. In a disease with this aggressive behaviour these aspects are of paramount importance.

The way forward:

- Develop integrated systems to measure the quality of care from the patients' viewpoint with specific tools and their monitoring through mobile apps. This may reduce the need for hospital stays, improve compliance with the treatment plan and ultimately prognosis.

- Digitalize the whole health care process. This may result in an optimization of costs and resources and in a reduced burden for caregivers. Integrating a "patient oriented" measure of the quality of care is likely to improve not only the quality of life but also engagement and eventually the clinical outcomes.

References & more details in the review article in UEG Journal:

Michl, P, Löhr, M, Neoptolemos, JP, Capurso, G, Rebours, V, Malats, N, et al. UEG position paper on pancreatic cancer. Bringing pancreatic cancer to the 21st century: prevent, detect, and treat the disease earlier and better. *United European Gastroenterol J*. 2021; 9 (7): 860– 871.