**Name of Journal:** *World Journal of Gastrointestinal Surgery*

**Manuscript NO:** 79435

**Manuscript Type:** EDITORIAL

**Hot topics in pancreatic cancer management**

Caputo D. Pancreatic cancer

Damiano Caputo

**Damiano Caputo,** Department of General Surgery, Fondazione Policlinico Universitario Campus Bio-Medico, Rome 00128, Italy

**Damiano Caputo,** General Surgery Research Unit, University Campus Bio-Medico di Roma, Rome 00128, Italy

**Author contributions:** Caputo D finished the concept, writing and critical analysis of this manuscript.

**Corresponding author: Damiano Caputo, FACS, MD, Associate Professor,** Department of General Surgery, Fondazione Policlinico Universitario Campus Bio-Medico, Via Alvaro del Portillo, 200, Rome 00128, Italy. d.caputo@policlinicocampus.it

**Received:** August 27, 2022

**Revised:** October 27, 2022

**Accepted:** January 17, 2023

**Published online:** February 27, 2023

**Abstract**

Pancreatic ductal adenocarcinoma (PDAC) is a sneaky and lethal disease burdened by poor prognosis. PDAC is often detected too late to be successfully cured, and it has been estimated that it will be a leading cause of cancer-related deaths in the near future. During the last decade, multimodal treatments involving surgery, chemotherapy and radiotherapy have contributed to improving the prognosis of this disease; however, long-term results are still not satisfactory. Postoperative morbidity and mortality rates remain high, and systemic treatments are burdened by toxicity in both neoadjuvant and adjuvant settings. Advancements in technologies, targeted therapies, immunotherapy and PDAC microenvironment modulation strategies may represent useful potential weapons in the future. Nevertheless, in the fight against this dreadful disease, there is an urgent need for new, cheap and user-friendly tools for early detection. In this field, promising results have been found in nanotechnologies and “omics” analyses that search for new biomarkers to be used in primary and secondary prevention. However, there are many issues that need to be solved before considering these tools in daily clinical practice. This editorial reported the state of the art of pancreatic cancer management.

**Key Words:** Pancreatic cancer; Pancreatic ductal adenocarcinoma; Nanotechnology; Neoadjuvant therapy; Adjuvant therapy; Omics

**©The** **Author(s) 2023.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation:** Caputo D. Hot topics in pancreatic cancer management. *World J Gastrointest Surg* 2023; 15(2): 121-126

**URL**: https://www.wjgnet.com/1948-9366/full/v15/i2/121.htm

**DOI**: https://dx.doi.org/10.4240/wjgs.v15.i2.121

**Core Tip:** The purpose of this editorial was to provide an up-to-date summary of pancreatic cancer management. The current state of multimodal therapies and the increasingly urgent need for development of tools for early diagnosis were summarized. The editorial also presented the high quality papers in the fields of basic, clinical, preventive and translational medicine that will help further investigations focused on this topic.

**INTRODUCTION**

Pancreatic ductal adenocarcinoma (PDAC), one of the biggest killers among solid tumors, is set to become the second leading cause of cancer-related deaths in the near future[1]. In recent years, a lot has been done in order to improve the prognosis of PDAC. However, multimodal treatments combining surgery, still considered the gold standard of care, with chemotherapy and radiotherapy in neoadjuvant or adjuvant settings have allowed only a little progress towards better outcomes. Therefore, according to Torphy *et al*[2], pancreatic cancer management still has a long way to go.

Because of the very aggressive biology of PDAC and its indolent behavior in the early stage, the battle against this dreadful disease will be fought on the fields of prevention and early detection and improving the molecular understanding of PDAC[2]. Nevertheless, the assessment of more effective systemic treatments and strategies to improve surgical outcomes will represent an important step forward in the management of pancreatic cancer. Furthermore, much is expected from developments in targeted therapies and modulation of tumor microenvironment to improve the efficacy of immunotherapies[3].

The purpose of this editorial was to provide an up-to-date summary on pancreatic cancer management. The current state of multimodal therapies and the increasingly urgent need for development of tools for early diagnosis were also summarized.

***Early detection and advances in clinical diagnosis***

Given that risk factors (*e.g.,* cigarette smoking, obesity, diabetes) and genetic predisposition contribute to the development of pancreatic cancer[4], it is clear that the control of the above-mentioned risk factors represents the first, although insufficient, step to prevent PDAC. PDAC is preceded by pancreatic intraepithelial neoplasia, intraductal papillary mucinous neoplasm and mucinous cystic neoplasm, and follow-up guidelines of these conditions have been widely reported. On the other hand, subjects at higher risk for familial PDAC can be successfully screened by endoscopic ultrasound and magnetic resonance cholangiopancreatography[5]. One of the main issues to be solved is the identification of individuals who are at risk of the disease even in absence of positive familiar history[6].

Clearly, invasive and expensive diagnostic investigations cannot be applied indiscriminately on a large scale for asymptomatic adults[7]. On this basis, there is still an urgent need for tools for early diagnosis of pancreatic cancer that fulfill the criteria of reliability, reproducibility and cost control required by the World Health Organization[8].

Recent technological advances have led to the revision of the so called Affordable-Sensitive-Specific-User Friendly-Rapid-Equipment Free and Delivered criteria proposed in the early 2000s to the Real Time Connectivity-Ease of specimen collection-Affordable-Sensitive-Specific-User Friendly-Rapid-Equipment Free and Delivered criteria[9]. On this basis, it is clear that the development of new tools to be used for early detection of PDAC must consider the ease of collection of biological samples such as blood, saliva, urine, *etc.*

In this scenario, our group together with the researchers of the Department of Molecular Medicine of Sapienza University of Rome were among the first to exploit the potential of nanotechnologies to assist the early diagnosis of pancreatic cancer[10]. When nanoparticles interact with human fluids (*e.g.,* plasma), a shield of molecules, mostly proteins, cover them and form the so-called biomolecular corona or protein corona. Protein corona-based technologies proved their efficacy in distinguishing pancreatic cancer patients from controls with a high rate of sensitivity (up to 85%) and specificity (up to 100%)[11].

More recently, in an attempt to make nanoparticle-based diagnostic technology even more streamlined and reproducible, approaches based on the use of magnetic levitation of nanoparticles coated by personalized protein corona have been proposed. Magnetic levitation (MagLev) may overcome protein corona analysis limitations (*e.g.,* isolation of plasma proteins from nanoparticles), boosting reproducibility and clinical translation of these technologies[12].

In the attempt to search for new biomarkers to be used in the early detection of pancreatic cancer, other remarkable results have been provided by different “omics” technologies (*e.g.,* genomics, epigenomics, non-coding RNA, metabolomics, liquid biopsy, *etc*). Studies in these fields identified many biomarkers that proved their utility alone or in panels with different combinations. Unfortunately, their application in daily clinical practice is still a long way off as large-scale validation studies are lacking, and these technologies require expensive and complex equipment[13].

As mutations in *KRAS*, *GNAS*, *CDKN2A*, *TP53* and *SMAD4* have been shown in different staged PDAC and precancerous lesions and due to “omics” analysis advancements, the opportunity of DNA-based molecular approaches for early PDAC detection is also gaining momentum. These approaches have the advantages of being based on the assessment of genetic mutations on easily obtainable samples (*e.g.,* blood, plasma)[14].

***Treatment guidelines: Standards and challenges***

**Surgery:** Surgical resection still represents the cornerstone of pancreatic cancer treatment. However, despite recent technological improvements and the increasing diffusion of the minimally invasive approaches, morbidity and mortality rates remain significant even in high-volume centers[15].

**Neoadjuvant treatments:** The growing number of studies supporting vascular resections, when indicated, together with the promising results obtained with neoadjuvant therapies have undoubtedly increased the rate of PDACs that are eligible for surgical treatment. Although vascular resection, mainly when arteries are involved, should be reserved in selected cases and performed in high-volume hospitals[16], neoadjuvant treatments are gaining consensus in both the scientific community and clinical practice.

In borderline resectable PDACs, higher rates of R0 resections and longer disease-free and overall survival rates have been reported when FOLFIRINOX-based neoadjuvant treatments are used[17]. Recently, a prospective multicenter phase 2 trial demonstrated promising results when gemcitabine plus nab-paclitaxel chemotherapy were administered before surgery[18].Even though the data supporting the use of neoadjuvant therapies in resectable PDACs are more limited, this strategy is proposed in patients with “biological” borderline resectable tumors (*e.g.,* radiological resectable PDACs with elevated levels of Ca-199)[19].

In this field, a randomized phase 2 clinical trial showed the efficacy of perioperative regimens of gemcitabine plus nab-paclitaxel in terms of disease-free survival[20]. Nonetheless, for both resectable and borderline resectable PDACs, the Dutch Randomized Phase III PREOPANC Trial showed the efficacy of neoadjuvant treatments in terms of R0 resections and disease-free survival in the absence of significant improvement of overall survival rates[21]. The other side of the coin is that patients undergo significant surgical procedures for more advanced disease after chemotherapy and radiotherapy treatments contributing to high toxicity[22].

Reduction of complications, prevention and mitigation of the effects of postoperative pancreatic fistula, optimization of neoadjuvant therapies with careful selection of patients who will actually benefit from these treatments and identification of drugs and therapeutic regimens with a more favorable balance between efficacy and toxicity will represent a turning point in the management of pancreatic cancer[23,24].

**Adjuvant treatments and metastatic disease:** Adjuvant chemotherapy plays an important role in the treatment of pancreatic cancer. In 2013, results of the Conko-001 trial confirmed the usefulness of adjuvant chemotherapy in improving the disease-free survival rates of surgically removed PDAC[25].

Later, gemcitabine alone proved to offer the same oncological outcomes with lower toxicity when compared to 5-fluorouracil[26]. More recently, FOLFIRINOX-based regimens have led to significant improvement in overall survival, but because of their toxicity they can be administered to only very fit patients after surgery[27]. Based on the recent data reported by Choi *et al*[28], 5-fluoruracil regimens should be considered the optimal adjuvant treatment in patients with borderline resectable and locally advanced PDAC who already received neoadjuvant FOLFIRINOX. The PRODIGE 24/Canadian Cancer Trials Group PA6 just demonstrated that in resected PDACs, adjuvant FOLFIRINOX allows significantly longer survival when compared with gemcitabine[29].

Furthermore, there is increasing evidence in favor of the use of FOLFIRINOX for patients with unresectable metastatic disease[3]. On this basis, it is clear that advances have been made in the field of adjuvant therapy, but more investigations are needed. Improvement of oncological outcomes and significant reduction of toxicity are expected from targeted therapies and immunotherapy[30].

**DISCUSSION**

Torphy *et al*[2] has stated that much has been done but the way to win the battle against this cancer is still long. Early detection and novel therapeutic strategies represent the most urgent issues that need to be tackled. Hence, it is necessary to develop patient models and identify cheap, user-friendly and reproducible biomarkers that can be applied in daily clinical practice to assess the most effective treatment for each patient with PDAC.

In this scenario, translational research is rapidly gaining ground; organoid *ex vivo* models of PDAC can be achieved from small biopsies and may represent a turning point for precision medicine approaches in cases of resectable, locally advanced and metastatic PDAC[31]. In other words, the time seems ripe to collect all the knowledge acquired in the preclinical field over the last few decades and to recommend models of PDAC in different stages that can be used to improve our diagnostic and therapeutic strategies[32].

**CONCLUSION**

In the very near future, we will be increasingly called upon to fight the battle against PDAC. Improvements of surgical outcomes, careful selection of patients for neoadjuvant treatments and vascular resections and reduction of the toxicity of adjuvant therapies are unquestionably needed. However, in order to increase the odds of winning the battle against this lethal disease, the real gap to be filled is the assessment of cheap and easily reproducible strategies for the screening and early detection of PDAC. Indeed, the aim of this special issue was to collect quality studies in the fields of basic, clinical, preventive and translational medicine that will further help investigations focus on these topics (Table 1).

**REFERENCES**

1 **Neoptolemos JP**, Kleeff J, Michl P, Costello E, Greenhalf W, Palmer DH. Therapeutic developments in pancreatic cancer: current and future perspectives. *Nat Rev Gastroenterol Hepatol* 2018; **15**: 333-348 [PMID: 29717230 DOI: 10.1038/s41575-018-0005-x]

2 **Torphy RJ**, Fujiwara Y, Schulick RD. Pancreatic cancer treatment: better, but a long way to go. *Surg Today* 2020; **50**: 1117-1125 [PMID: 32474642 DOI: 10.1007/s00595-020-02028-0]

3 **Mizrahi JD**, Surana R, Valle JW, Shroff RT. Pancreatic cancer. *Lancet* 2020; **395**: 2008-2020 [PMID: 32593337 DOI: 10.1016/S0140-6736(20)30974-0]

4 **Antwi SO**, Oberg AL, Shivappa N, Bamlet WR, Chaffee KG, Steck SE, Hébert JR, Petersen GM. Pancreatic cancer: associations of inflammatory potential of diet, cigarette smoking and long-standing diabetes. *Carcinogenesis* 2016; **37**: 481-490 [PMID: 26905587 DOI: 10.1093/carcin/bgw022]

5 **Goggins M**, Overbeek KA, Brand R, Syngal S, Del Chiaro M, Bartsch DK, Bassi C, Carrato A, Farrell J, Fishman EK, Fockens P, Gress TM, van Hooft JE, Hruban RH, Kastrinos F, Klein A, Lennon AM, Lucas A, Park W, Rustgi A, Simeone D, Stoffel E, Vasen HFA, Cahen DL, Canto MI, Bruno M; International Cancer of the Pancreas Screening (CAPS) consortium. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. *Gut* 2020; **69**: 7-17 [PMID: 31672839 DOI: 10.1136/gutjnl-2019-319352]

6 **McGuigan A**, Kelly P, Turkington RC, Jones C, Coleman HG, McCain RS. Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment and outcomes. *World J Gastroenterol* 2018; **24**: 4846-4861 [PMID: 30487695 DOI: 10.3748/wjg.v24.i43.4846]

7 **Pereira SP**, Oldfield L, Ney A, Hart PA, Keane MG, Pandol SJ, Li D, Greenhalf W, Jeon CY, Koay EJ, Almario CV, Halloran C, Lennon AM, Costello E. Early detection of pancreatic cancer. *Lancet Gastroenterol Hepatol* 2020; **5**: 698-710 [PMID: 32135127 DOI: 10.1016/S2468-1253(19)30416-9]

8 **Land KJ**, Boeras DI, Chen XS, Ramsay AR, Peeling RW. REASSURED diagnostics to inform disease control strategies, strengthen health systems and improve patient outcomes. *Nat Microbiol* 2019; **4**: 46-54 [PMID: 30546093 DOI: 10.1038/s41564-018-0295-3]

9 **Bernabé-Ortiz A**, Zafra-Tanaka JH, Moscoso-Porras M, Sampath R, Vetter B, Miranda JJ, Beran D. Diagnostics and monitoring tools for noncommunicable diseases: a missing component in the global response. *Global Health* 2021; **17**: 26 [PMID: 33750391 DOI: 10.1186/s12992-021-00676-6]

10 **Caputo D**, Caracciolo G. Nanoparticle-enabled blood tests for early detection of pancreatic ductal adenocarcinoma. *Cancer Lett* 2020; **470**: 191-196 [PMID: 31783084 DOI: 10.1016/j.canlet.2019.11.030]

11 **Caputo D**, Pozzi D, Farolfi T, Passa R, Coppola R, Caracciolo G. Nanotechnology and pancreatic cancer management: State of the art and further perspectives. *World J Gastrointest Oncol* 2021; **13**: 231-237 [PMID: 33889275 DOI: 10.4251/wjgo.v13.i4.231]

12 **Digiacomo L**, Quagliarini E, La Vaccara V, Coppola A, Coppola R, Caputo D, Amenitsch H, Sartori B, Caracciolo G, Pozzi D. Detection of Pancreatic Ductal Adenocarcinoma by Ex Vivo Magnetic Levitation of Plasma Protein-Coated Nanoparticles. *Cancers (Basel)* 2021; **13** [PMID: 34680304 DOI: 10.3390/cancers13205155]

13 **Zhou B**, Xu JW, Cheng YG, Gao JY, Hu SY, Wang L, Zhan HX. Early detection of pancreatic cancer: Where are we now and where are we going? *Int J Cancer* 2017; **141**: 231-241 [PMID: 28240774 DOI: 10.1002/ijc.30670]

14 **Singhi AD**, Wood LD. Early detection of pancreatic cancer using DNA-based molecular approaches. *Nat Rev Gastroenterol Hepatol* 2021; **18**: 457-468 [PMID: 34099908 DOI: 10.1038/s41575-021-00470-0]

15 **Miyasaka Y**, Ohtsuka T, Nakamura M. Minimally invasive surgery for pancreatic cancer. *Surg Today* 2021; **51**: 194-203 [PMID: 32857251 DOI: 10.1007/s00595-020-02120-5]

16 **Małczak P**, Sierżęga M, Stefura T, Kacprzyk A, Droś J, Skomarovska O, Krzysztofik M, Major P, Pędziwiatr M. Arterial resections in pancreatic cancer – Systematic review and meta-analysis. *HPB (Oxford)* 2020; **22**: 961-968 [PMID: 32360186 DOI: 10.1016/j.hpb.2020.04.005]

17 **Gorbudhun R**, Patel PH, Hopping E, Doyle J, Geropoulos G, Mavroeidis VK, Kumar S, Bhogal RH. Neoadjuvant Chemotherapy-Chemoradiation for Borderline-Resectable Pancreatic Adenocarcinoma: A UK Tertiary Surgical Oncology Centre Series. *Cancers (Basel)* 2022; **14** [PMID: 36230600 DOI: 10.3390/cancers14194678]

18 **Ikenaga N**, Miyasaka Y, Ohtsuka T, Nakata K, Adachi T, Eguchi S, Nishihara K, Inomata M, Kurahara H, Hisaka T, Baba H, Nagano H, Ueki T, Noshiro H, Tokunaga S, Ishigami K, Nakamura M; Kyushu Study Group of Treatment for Pancreatobiliary Cancer. A Prospective Multicenter Phase II Trial of Neoadjuvant Chemotherapy with Gemcitabine Plus Nab-Paclitaxel for Borderline Resectable Pancreatic Cancer with Arterial Involvement. *Ann Surg Oncol* 2023; **30**: 193-202 [PMID: 36207481 DOI: 10.1245/s10434-022-12566-1]

19 **Coppola A**, La Vaccara V, Farolfi T, Fiore M, Cammarata R, Ramella S, Coppola R, Caputo D. Role of CA 19.9 in the Management of Resectable Pancreatic Cancer: State of the Art and Future Perspectives. *Biomedicines* 2022; **10** [PMID: 36140192 DOI: 10.3390/biomedicines10092091]

20 **Seufferlein T**, Uhl W, Kornmann M, Algül H, Friess H, König A, Ghadimi M, Gallmeier E, Bartsch DK, Lutz MP, Metzger R, Wille K, Gerdes B, Schimanski CC, Graupe F, Kunzmann V, Klein I, Geissler M, Staib L, Waldschmidt D, Bruns C, Wittel U, Fichtner-Feigl S, Daum S, Hinke A, Blome L, Tannapfel A, Kleger A, Berger AW, Kestler AMR, Schuhbaur JS, Perkhofer L, Tempero M, Reinacher-Schick AC, Ettrich TJ. Perioperative or only adjuvant gemcitabine plus nab-paclitaxel for resectable pancreatic cancer (NEONAX) – a randomized phase II trial of the AIO pancreatic cancer group. *Ann Oncol* 2023; **34**: 91-100 [PMID: 36209981 DOI: 10.1016/j.annonc.2022.09.161]

21 **Versteijne E**, Suker M, Groothuis K, Akkermans-Vogelaar JM, Besselink MG, Bonsing BA, Buijsen J, Busch OR, Creemers GM, van Dam RM, Eskens FALM, Festen S, de Groot JWB, Groot Koerkamp B, de Hingh IH, Homs MYV, van Hooft JE, Kerver ED, Luelmo SAC, Neelis KJ, Nuyttens J, Paardekooper GMRM, Patijn GA, van der Sangen MJC, de Vos-Geelen J, Wilmink JW, Zwinderman AH, Punt CJ, van Eijck CH, van Tienhoven G; Dutch Pancreatic Cancer Group. Preoperative Chemoradiotherapy Versus Immediate Surgery for Resectable and Borderline Resectable Pancreatic Cancer: Results of the Dutch Randomized Phase III PREOPANC Trial. *J Clin Oncol* 2020; **38**: 1763-1773 [PMID: 32105518 DOI: 10.1200/JCO.19.02274]

22 **Karunakaran M**, Barreto SG. Surgery for pancreatic cancer: current controversies and challenges. *Future Oncol* 2021; **17**: 5135-5162 [PMID: 34747183 DOI: 10.2217/fon-2021-0533]

23 **Cheng Y**, Briarava M, Lai M, Wang X, Tu B, Cheng N, Gong J, Yuan Y, Pilati P, Mocellin S. Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction for the prevention of postoperative pancreatic fistula following pancreaticoduodenectomy. *Cochrane Database Syst Rev* 2017; **9**: CD012257 [PMID: 28898386 DOI: 10.1002/14651858.CD012257.pub2]

24 **Fiore M**, Ramella S, Valeri S, Caputo D, Floreno B, Trecca P, Trodella LE, Trodella L, D’Angelillo RM, Coppola R. Phase II study of induction chemotherapy followed by chemoradiotherapy in patients with borderline resectable and unresectable locally advanced pancreatic cancer. *Sci Rep* 2017; **7**: 45845 [PMID: 28378800 DOI: 10.1038/srep45845]

25 **Oettle H**, Neuhaus P, Hochhaus A, Hartmann JT, Gellert K, Ridwelski K, Niedergethmann M, Zülke C, Fahlke J, Arning MB, Sinn M, Hinke A, Riess H. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. *JAMA* 2013; **310**: 1473-1481 [PMID: 24104372 DOI: 10.1001/jama.2013.279201]

26 **Neoptolemos JP**, Palmer DH, Ghaneh P, Psarelli EE, Valle JW, Halloran CM, Faluyi O, O’Reilly DA, Cunningham D, Wadsley J, Darby S, Meyer T, Gillmore R, Anthoney A, Lind P, Glimelius B, Falk S, Izbicki JR, Middleton GW, Cummins S, Ross PJ, Wasan H, McDonald A, Crosby T, Ma YT, Patel K, Sherriff D, Soomal R, Borg D, Sothi S, Hammel P, Hackert T, Jackson R, Büchler MW; European Study Group for Pancreatic Cancer. Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomized, phase 3 trial. *Lancet* 2017; **389**: 1011-1024 [PMID: 28129987 DOI: 10.1016/S0140-6736(16)32409-6]

27 **Ghosn M**, Kourie HR, El Rassy E, Haddad FG, Hanna C, El Karak F, Nasr D. Where does chemotherapy stands in the treatment of ampullary carcinoma? A review of literature. *World J Gastrointest Oncol* 2016; **8**: 745-750 [PMID: 27795814 DOI: 10.4251/wjgo.v8.i10.745]

28 **Choi JH**, Kim MK, Lee SH, Park JW, Park N, Cho IR, Ryu JK, Kim YT, Jang JY, Kwon W, Kim H, Paik WH. Proper adjuvant therapy in patients with borderline resectable and locally advanced pancreatic cancer who had received neoadjuvant FOLFIRINOX. *Front Oncol* 2022; **12**: 945829 [PMID: 36226066 DOI: 10.3389/fonc.2022.945829]

29 **Conroy T**, Castan F, Lopez A, Turpin A, Ben Abdelghani M, Wei AC, Mitry E, Biagi JJ, Evesque L, Artru P, Lecomte T, Assenat E, Bauguion L, Ychou M, Bouché O, Monard L, Lambert A, Hammel P; Canadian Cancer Trials Group and the Unicancer-GI–PRODIGE Group. Five-Year Outcomes of FOLFIRINOX *vs* Gemcitabine as Adjuvant Therapy for Pancreatic Cancer: A Randomized Clinical Trial. *JAMA Oncol* 2022; **8**: 1571-1578 [PMID: 36048453 DOI: 10.1001/jamaoncol.2022.3829]

30 **Liu X**, Li Z, Wang Y. Advances in Targeted Therapy and Immunotherapy for Pancreatic Cancer. *Adv Biol (Weinh)* 2021; **5**: e1900236 [PMID: 33729700 DOI: 10.1002/adbi.201900236]

31 **Tiriac H**, Plenker D, Baker LA, Tuveson DA. Organoid models for translational pancreatic cancer research. *Curr Opin Genet Dev* 2019; **54**: 7-11 [PMID: 30844513 DOI: 10.1016/j.gde.2019.02.003]

32 **Connor AA**, Gallinger S. Pancreatic cancer evolution and heterogeneity: integrating omics and clinical data. *Nat Rev Cancer* 2022; **22**: 131-142 [PMID: 34789870 DOI: 10.1038/s41568-021-00418-1]

**Footnotes**

**Conflict-of-interest statement:** The author declares that he has no conflicts of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/Licenses/by-nc/4.0/>

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** August 27, 2022

**First decision:** October 21, 2022

**Article in press:** January 17, 2023

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** Italy

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C, C, C

Grade D (Fair): D, D

Grade E (Poor): 0

**P-Reviewer:** Hamaya Y, Japan; Kim SC, South Korea; Kitamura K, Japan; Song B, China **S-Editor:** Wang JJ **L-Editor:** Filipodia **P-Editor:** Wang JJ

**Table 1 Most relevant topics in pancreatic ductal adenocarcinoma management with their current challenges and potential further perspectives**

|  |  |  |
| --- | --- | --- |
| **Topic** | **Challenges** | **Potential further perspectives** |
| Prevention and early detection | Identification of high risk subjects | Nanotechnology |
| Identification of novel biomarkers and signatures that satisfy the WHO REASSURED criteria | Omics technologies |
| Surgical treatment | Reduction of morbidity and mortality rates | Optimization of vascular resection in high skilled hospitals |
| Neoadjuvant treatments | Reduction of toxicity | Careful selection of fit patients |
| Identification of therapeutic regimens with favorable balance between efficacy and toxicity |
| Adjuvant treatments | Improvement of oncological outcomes | Targeted therapies |
| Significant reduction of toxicity | Immunotherapy |
| Biology and behavior | Lack of patient models of the tumor in order to improve translational medicine | Organoid *ex vivo* models |

REASSURED: Real Time Connectivity-Ease of specimen collection-Affordable- Sensitive-Specific-User Friendly-Rapid-Equipment Free and Delivered; WHO: World Health Organization.



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** bpgoffice@wjgnet.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2023 Baishideng Publishing Group Inc. All rights reserved.**