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# UROPANC Trial: Unveiling a New Era in Pancreatic Cancer Detection and Treatment

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## Abstract

This article explores the UROPANC trial's innovative approach to early detection and treatment of Pancreatic Ductal Adenocarcinoma (PDAC), a cancer known for its late diagnosis. Led by Professor Crnogorac-Jurcevic at the Queen Mary University of London, the trial is a beacon of hope in oncology, potentially revolutionising PDAC management. At its core is the PancRISK algorithm, which utilises a urinary biomarker panel including REG1B, LYVE1, and TFF1 to detect PDAC cancer before metastasis. These biomarkers present a non-invasive, cost-effective method for early-stage PDAC detection. Involving over 3,000 symptomatic and asymptomatic participants, the trial aims to validate these biomarkers in conjunction with the traditional CA19-9 marker. This method could significantly enhance early detection, improving treatment outcomes and survival rates. This article delves into the trial's methodology and the broader implications of its findings. The UROPANC trial represents a significant leap in PDAC management, and a paradigm shift in the detection and treatment of one of the most challenging forms of cancer.

## The Silent Killer: Pancreatic Ductal Adenocarcinoma

Pancreatic ductal adenocarcinoma remains one of the most challenging cancers to detect and treat. PDAC's five-year survival rate is less than 7%[10]. It is a disease that often remains hidden until it is too late, making early detection not just a medical challenge but a dire necessity. It is the fifth biggest cancer killer in the UK and, by 2030, is predicted to overtake breast cancer, the fourth largest cancer killer [9].

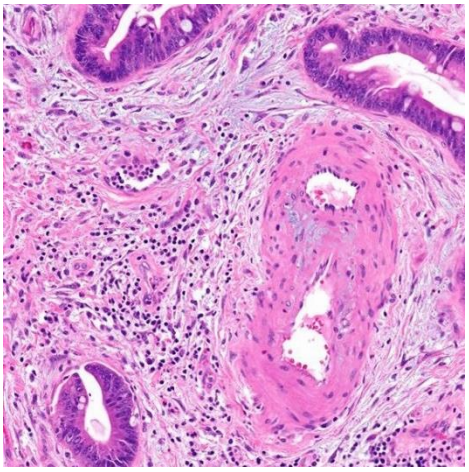

Figure 1. Histological image of typical glands immediately adjacent to artery depicted by haematoxylin and eosin stain[15].

## UROPANC Trial: A Ray of Hope



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The UROPANC trial, led by Professor Crnogorac-Jurcevic at Queen Mary University of London, marks a potential breakthrough in early PDAC detection. The novel urinary biomarker panel originated from findings where patient urine samples were used, uncovering the discovery of the original three-protein biomarker panel, LYVE-1, REG1A, and TFF1[12]. These biomarkers can detect patients with early-stage PDAC, and their small-scale study reported miRNA in urine for this early detection[12]. The existing urinary panel was improved by substituting REG1A with REG1B to enhance the performance of the biomarker panel[6]. With PanRISK, the UROPANC trial aims to identify PDAC at a more resectable stage (stages I and II)[2].

## Why This Matters: The Challenge of PDAC Diagnosis

The insidious nature of PDAC lies in its obscurity and asymptomatic progression[14]. The pancreas, nestled deep within the abdomen, betrays little of the turmoil within until the cancer has advanced significantly. Due to the tumour being near-impossible to see or feel during routine medical examinations, 80% of PC patients get diagnosed, often when cancer has metastasised (physiological symptoms appear), and the options for effective treatment diminish drastically. The average survival is only 2-6 months[9]. This stark mortality rate underscores the urgent need for a reliable early detection method, which the UROPANC trial seeks to provide . The PancRISK algorithm is used in conjunction with CA19-9 as a tool for diagnosis for detecting PDAC up to 2 years before diagnosis[5]. The cancer can be found up to 2 years before diagnosis, so surgical intervention can be soon employed to target the cancer at its emergence.

## Decoding the Biomarker Panel: REG1B, LYVE1, TFF1

Central to the trial is the PancRISK algorithm, which employs biomarkers Regenerating Family Member 1 Beta (REG1B), Lymphatic Vessel Endothelial Hyaluronan Receptor 1 (LYVE1), and Trefoil Factor 1 (TFF1)[2]. These markers in urine could revolutionise PDAC detection by signalling the disease's presence early before symptoms manifest. The biomarker panel incorporated in PancRISK may improve early diagnosis and patient outcomes. To delve briefly into the mechanism, REG1B is an early indicator of pancreatic issues –secreted by pancreatic cells in response to injury or inflammation. In the context of PDAC, elevated levels of REG1B may indicate abnormal cellular activity, tissue damage, or the presence of a tumour. LYVE1 detects abnormal activity, such as lymphangiogenesis, which may contribute to tumour growth, invasion, and metastasis by providing a route for cancer cells to spread to distant sites[13]. While TFF1 indicates a response to potential threats such as tissue damage, as PDAC often arises from precancerous lesions or damaged pancreatic tissue. TFF1 may be involved in repairing and maintaining the integrity of the pancreatic mucosa in response to tissue damage, resembling the body's way of defending itself[16]. Together, these biomarkers contribute to the early detection of PDAC by providing crucial signals that can alert healthcare professionals to the presence of the disease.



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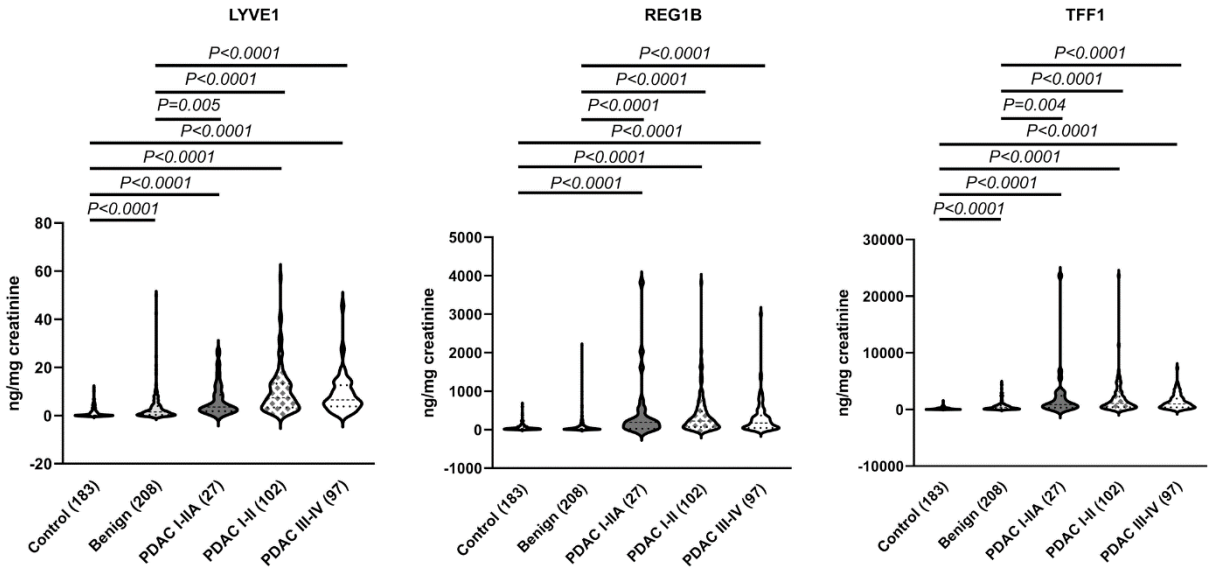


Figure 2. The levels of the 3 biomarkers, REG1B, LYVE1, TFF1, in control, benign, and pancreatic ductal adenocarcinoma (PDAC) samples. Violin plots are illustrated for each protein. The number of samples per group is shown in parentheses. All data were creatinine normalised. Upper bars: Kruskal–Wallis test, Dunn's multiple comparisons[7].

## Trial Dynamics: Objectives and Methodology

By enrolling over 3,000 participants who are both symptomatic and asymptomatic, the UROPANC trial has set out to validate these biomarkers independently and in conjunction with CA19-9, another marker typically associated with pancreatic cancer[4]. Compared to CA19-9, which primarily measures the levels of a specific antigen associated with pancreatic cancer, the biomarkers REG1B, LYVE1, and TFF1 target distinct biological pathways involved in pancreatic cancer pathogenesis. The biomarkers and CA19-9, in conjunction, could provide a more comprehensive assessment of PDAC by capturing different aspects of the disease development and enhancing the accuracy of PancRISK. This comprehensive approach aims to solidify the reliability and effectiveness of the biomarker panel. The trial's methodology involves a detailed comparison of biomarker readings with imaging and histological data to validate accuracy and reliability[3].

## Advancing Beyond Current Limitations

CA19-9, a current standalone biomarker diagnostic method, can result in false positives – elevated levels are seen in non-pancreatic conditions like liver disease. Increased false positivity was found in the presence of obstructive jaundice (10-60%)[1]. Also, it is not specific to pancreatic cancer as there are elevated levels in other types of cancer, such as hepatocellular carcinoma. CA19-9 cannot distinguish between PDAC and other conditions like distal cholangiocarcinoma (DCCA)[8]. DDCA and PDCA are anatomically proximal, symptom-overlapping, and histologically similar; their biomarkers overlap. This lack of specificity can lead to misdiagnoses and delayed treatment. The UROPANC trial's biomarker panel aims to address these shortcomings, offering a more precise and early detection tool. For patients, the implications of the UROPANC trial are profound. Early detection can mean the difference between a terminal diagnosis and a treatable condition. It opens the door to earlier interventions, including surgery, which could significantly extend life expectancy and improve the quality of life for PDAC patients. However, the need for patient lifetime treatment monitoring would depend on individual patient factors, the type and stage of cancer, and the risk of recurrence; UROPANC would allow healthcare providers to personalise a patient treatment plan based on the diagnosis. The benefits would reflect in the socioeconomic factors; this highly accurate and non-invasive diagnostic test would bridge the gap of the clinical need for screening patients at risk: proactively tackling the disease before symptoms occur. Consequently, there would be less strain on resources needed in diagnostic care and treatment, and the patient backlog would decrease as PancRISK and the urinary biomarker panel offer a quick and inexpensive method. Treatment would mean less invasive procedures, leading to higher patient satisfaction.



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## Potential Impact and Future Prospects

Successful validation of this biomarker panel could revolutionise how PDAC is diagnosed and treated. It represents a leap towards more cost-effective and non-invasive detection methods, potentially significantly increasing the five-year survival rate. For decades, pancreatic cancer has been underfunded and only receives 3% of the UK cancer research budget[11]. Additionally, as the PancRISK algorithm uses the three-urinary-biomarker-panel to signal the presence of PDCA, the trial's findings could pave the way for similar breakthroughs in other types of cancer, broadening the horizon of cancer research and treatment. While it is a valuable tool for early detection through detecting the presence of levels of expression, it may not necessarily serve as a monitoring tool for ongoing assessment. Additional medical tests and evaluations may be required to assess the need for monitoring and ongoing assessment. Current research strives to validate the urinary biomarker panel to implement for clinical use.

## Conclusion: A Beacon of Hope in PDAC Battle

In conclusion, the UROPANC trial showcases a pivotal moment in the fight against pancreatic cancer. Its success could mark the beginning of a new era in which PDAC is no longer a silent killer but a detectable and treatable condition. This trial is more than a scientific endeavour; it symbolises a future filled with hope for patients and a new direction in cancer research.

## References


Ballehaninna, U. K., & Chamberlain, R. S. (2012). The clinical utility of serum CA 19-9 in the diagnosis, prognosis and management of pancreatic adenocarcinoma: An evidence based appraisal. *J Gastrointest Oncol*, *3*(2), 105-119. https://doi.org/10.3978/j.issn.2078-6891.2011.021

Blyuss, O., Zaikin, A., Cherepanova, V., Munblit, D., Kiseleva, E. M., Prytomanova, O. M., Duffy, S. W., & Crnogorac-Jurcevic, T. (2020). Development of PancRISK, a urine biomarker-based risk score for stratified screening of pancreatic cancer patients. *Br J Cancer*, *122*(5), 692-696. https://doi.org/10.1038/s41416-019-0694-0

Cancer Research UK. (2022). *Research on the use of urine biomarkers for early detection of pancreatic cancer*. Barts Cancer Institute. Retrieved 21/11/2023 from https://www.bartscancer.london/interviews/2022/11/research-on-the-use-of-urine-biomarkers-for-early-detection-of-pancreatic-cancer/

Crnogorac-Jurcevic, T. (2022). *New tests for early detection of pancreatic cancer offer significant hope*. Queen Mary University of London. Retrieved 29/11/2023 from https://www.qmul.ac.uk/research/featured-research/new-tests-for-early-detection-of-pancreatic-cancer-offer-significant-hope/

Debernardi, S., Blyuss, O., Rycyk, D., Srivastava, K., Jeon, C. Y., Cai, H., Cai, Q., Shu, X. O., & Crnogorac-Jurcevic, T. (2023). Urine biomarkers enable pancreatic cancer detection up to 2 years before diagnosis. *Int J Cancer*, *152*(4), 769-780. https://doi.org/10.1002/ijc.34287

Debernardi, S., O'Brien, H., Algahmdi, A. S., Malats, N., Stewart, G. D., Plješa-Ercegovac, M., Costello, E., Greenhalf, W., Saad, A., Roberts, R., Ney, A., Pereira, S. P., Kocher, H. M., Duffy, S., Blyuss, O., & Crnogorac-Jurcevic, T. (2020). A combination of urinary biomarker panel and PancRISK score for earlier detection of pancreatic cancer: A case–control study. *PLoS Medicine*, *17*(12), e1003489. https://doi.org/10.1371/journal.pmed.1003489

Debernardi, S. e. a. (2020). The levels of the 3 biomarkers in control, benign, and pancreatic ductal adenocarcinoma (PDAC) samples. In journal.pmed.1003489.g001 (Ed.), (Vol. 630.4x293.71). Plosmedicine: Journal pubmed.

Lv, T.-R., Wang, J.-M., Ma, W.-J., Hu, Y.-F., Dai, Y.-S., Jin, Y.-W., & Li, F.-Y. (2022). The consistencies and inconsistencies between distal cholangiocarcinoma and pancreatic ductal adenocarcinoma: A systematic review and meta-analysis [Systematic Review]. *Frontiers in Oncology*, *12*. https://doi.org/10.3389/fonc.2022.1042493




DOI: https://doi.org/10.57898/biosci.184

Pancreatic Cancer UK. (2015). *Pancreatic Cancer: Some Key Facts*. Pancreatic Cancer UK. Retrieved 26/11/2023 from https://www.pancreaticcancer.org.uk/wp-content/uploads/2020/10/mp-pancreatic-cancer-briefing-notes.pdf

Pancreatic Cancer UK. (2023). *Pancreatic Cancer Statistics*. Pancreatic Cancer UK. Retrieved 27/11/2023 from https://www.pancreaticcancer.org.uk/what-we-do/media-centre/pancreatic-cancer-statistics/

Pancreatic Cancer UK. (2023). *We fund research breakthroughs*. Retrieved 01/02/24 from https://www.pancreaticcancer.org.uk/what-we-do/research/

Radon, T. P., Massat, N. J., Jones, R., Alrawashdeh, W., Dumartin, L., Ennis, D., Duffy, S. W., Kocher, H. M., Pereira, S. P., Guarner , L., Murta-Nascimento, C., Real, F. X., Malats, N., Neoptolemos, J., Costello, E., Greenhalf, W., Lemoine, N. R., & Crnogorac-Jurcevic, T. (2015). Identification of a Three-Biomarker Panel in Urine for Early Detection of Pancreatic Adenocarcinoma. *Clinical Cancer Research*, *21*(15), 3512-3521. https://doi.org/10.1158/1078-0432.Ccr-14-2467

Shen, C. N., Goh, K. S., Huang, C. R., Chiang, T. C., Lee, C. Y., Jeng, Y. M., Peng, S. J., Chien, H. J., Chung, M. H., Chou, Y. H., Hsieh, C. C., Kulkarni, S., Pasricha, P. J., Tien, Y. W., & Tang, S. C. (2019). Lymphatic vessel remodeling and invasion in pancreatic cancer progression. *EBioMedicine*, *47*, 98-113. https://doi.org/10.1016/j.ebiom.2019.08.044

UCLA Health. (2022). *Pancreatic cancer is almost impossible to detect early*. UCLA Health. Retrieved 29/11/2023 from https://www.uclahealth.org/news/pancreatic-cancer-is-almost-impossible-to-detect-early

Wei Chen, M. D., Ph.D. (2021). Atypical glands immediately adjacent to artery. In pancreasductalChen002.jpg (Ed.), (Vol. 501x551). pathologyoutlines.com: Pathology outlines.

Yamaguchi, J., Yokoyama, Y., Kokuryo, T., Ebata, T., Enomoto, A., & Nagino, M. (2018). Trefoil factor 1 inhibits epithelial-mesenchymal transition of pancreatic intraepithelial neoplasm. *The Journal of Clinical Investigation*, *128*(8), 3619-3629. https://doi.org/10.1172/JCI97755


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