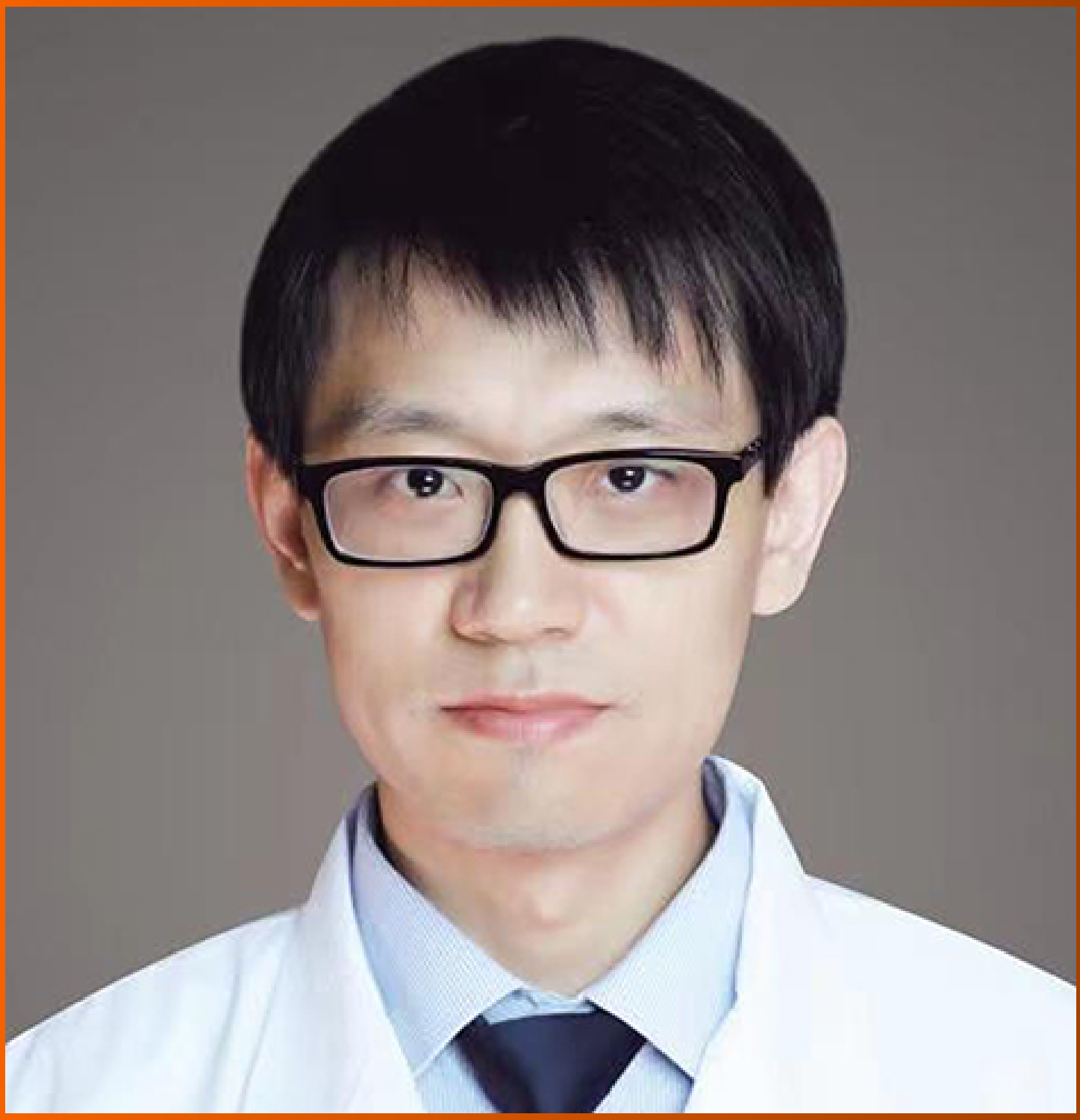
ISSN 2218-4333 (online)

World Journal of *Clinical Oncology*

World J Clin Oncol 2022 December 24; 13(12): 943-983



Published by Baishideng Publishing Group Inc

World Journal of Clinical Oncology

Contents

Monthly Volume 13 Number 12 December 24, 2022

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Cohort Study

LETTER TO THE EDITOR

World Journal of Clinical Oncology

Monthly Volume 13 Number 12 December 24, 2022

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Oncology*, Guangzhen Wu, MD, PhD, Postgraduate Tutor, Professor. First Affiliated Hospital of Dalian Medical University, No.222 Zhongshan Road, Xigang District, Dalian, Liaoning, 116000, China. wuguang0613@hotmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Oncology* (*WJCO*, *World J Clin Oncol*) is to provide scholars and readers from various fields of oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJCO mainly publishes articles reporting research results and findings obtained in the field of oncology and covering a wide range of topics including art of oncology, biology of neoplasia, breast cancer, cancer prevention and control, cancer-related complications, diagnosis in oncology, gastrointestinal cancer, genetic testing for cancer, gynecologic cancer, head and neck cancer, hematologic malignancy, lung cancer, melanoma, molecular oncology, neurooncology, palliative and supportive care, pediatric oncology, surgical oncology, translational oncology, and urologic oncology.

INDEXING/ABSTRACTING

The *WJCO* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 Journal Citation Indicator (JCI) for *WJCO* as 0.35.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Clinical Oncology

ISSN
ISSN 2218-4333 (online)

LAUNCH DATE
November 10, 2010

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Hiten RH Patel, Stephen Safe, Jian-Hua Mao, Ken H Young

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2218-4333/editorialboard.htm

PUBLICATION DATE
December 24, 2022

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Clinical Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Clin Oncol 2022 December 24; 13(12): 980-983

DOI: 10.5306/wjco.v13.i12.980

ISSN 2218-4333 (online)

LETTER TO THE EDITOR

Circulating tumour DNA in gastrointestinal cancer in clinical practice: Just a dream or maybe not?

Andrea Pretta, Eleonora Lai, Clelia Donisi, Dario Spanu, Pina Ziranu, Valeria Pusceddu, Marco Puzzoni, Elena Massa, Mario Scartozzi

Specialty type: Oncology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Kirchweger P, Austria; Liu S, China

Received: August 18, 2022
Peer-review started: August 18, 2022
First decision: September 5, 2022
Revised: September 16, 2022
Accepted: November 21, 2022
Article in press: November 21, 2022
Published online: December 24, 2022

Andrea Pretta, Eleonora Lai, Clelia Donisi, Dario Spanu, Pina Ziranu, Valeria Pusceddu, Marco Puzzoni, Elena Massa, Mario Scartozzi, Medical Oncology Unit, University Hospital and University of Cagliari, Monserrato 09042, Cagliari, Italy

Corresponding author: Eleonora Lai, MD, PhD, Staff Physician, Medical Oncology Unit, University Hospital and University of Cagliari, SS 554, km 4,500, bivio per Sestu, Monserrato 09042, Cagliari, Italy. eleonora.lai@unica.it

Abstract

The evaluation of circulating tumor DNA (ctDNA) is increasingly integrated into the management of diagnosis and treatment of gastrointestinal cancer as it represents an innovative and minimally invasive biomarker that could allow us to reach clinical needs not met yet in randomized clinical trials. Recent research provided an interesting overview of the role of circulating tumor DNA in gastric, biliary, liver, pancreatic, and colorectal cancer. Data regarding upper gastrointestinal tumors are currently not practice changing. Tumor detection rates are low in the early stages, while in advanced stages ctDNA is useful for molecular tracking evaluation. Most of the evidence comes from colorectal cancer studies, where ctDNA was evaluated both in the early and advanced stages with the post-surgery minimal residual disease assessment and the response assessment, respectively. ctDNA qualifies as a promising tool in the era of precision medicine, with potential applications in the entire management of gastrointestinal cancer patients. Further evidence is needed to establish which setting may be influenced greatly by liquid biopsy in clinical practice.

Key Words: Circulating tumor DNA; Gastrointestinal cancer; Liquid biopsy; Esophageal cancer; Gastric cancer; Liver cancer; Bile duct cancer; Pancreatic cancer; Colorectal cancer

Core Tip: Circulating tumor DNA is a promising tool in the era of precision medicine, with several potential applications in the entire management of gastrointestinal malignancies. Further evidence is needed to assess in which setting liquid biopsy might have a greater impact in clinical practice.

Citation: Pretta A, Lai E, Donisi C, Spanu D, Ziranu P, Pusceddu V, Puzzoni M, Massa E, Scartozzi M. Circulating tumour DNA in gastrointestinal cancer in clinical practice: Just a dream or maybe not? *World J Clin Oncol* 2022; 13(12): 980-983
URL: https://www.wjgnet.com/2218-4333/full/v13/i12/980.htm
DOI: https://dx.doi.org/10.5306/wjco.v13.i12.980

TO THE EDITOR

We read with great interest the minireview by Kirchweger *et al*[1], entitled "Circulating tumor DNA (ctDNA) for diagnosis, prognosis and treatment of gastrointestinal malignancies". This paper provides a comprehensive overview on available literature data regarding the potential role of ctDNA in the management of gastric, biliary tract, liver, pancreatic and colorectal cancer (CRC). The authors discuss the application of ctDNA detection from diagnosis to prognosis and treatment monitoring of each disease analysed, by critically presenting to the readers the advantages and limitations of this tool.

We strongly agree with authors that ctDNA represents an innovative, minimally invasive biomarker that might allow us to reach unmet clinical needs in clinical practice for gastrointestinal cancer patients if further validated in randomised clinical trials. Indeed, considering the dynamic nature of tumor biology and the genetic heterogeneity of diseases such as CRC, the serial assessments of biomarkers of interest through liquid biopsy might reflect the continuous changes of tumour itself and be useful to clinicians[2].

Notably, not a large amount of data is available about the application of ctDNA for diagnosis, as well as about its role in gastric and liver cancer. We greatly appreciate the authors' effort to analyse these particular aspects and cancer types which are not the main field of research for this topic.

Indeed, main evidences regard prognosis and treatment monitoring, both in early stages (detection of minimal residual disease) and in advanced stages. Moreover, the majority of evidences derive from CRC studies.

Recently, Bregni *et al*[3] showed that baseline ctDNA was an independent prognostic factor for disease free survival (HR 3.35, 95%CI: 1.15-9.77, P = 0.03) in stage III CRC patients treated with neoadjuvant conventional 5-fluorouracil, oxaliplatin and folinic acid (FOLFOX) followed by surgery +/- adjuvant FOLFOX in the PePiTA trial[4]. These findings derive from a small sample size (80 patients) but represent a starting point needing to be confirmed in larger trials focusing on early-stage CRC.

Surely, as highlighted by the authors, ctDNA has been extensively studied for tailoring treatment with anti-EGFR in further lines for RAS wild type metastatic CRC[5]. Our group recently explored the liquid biopsy-driven cetuximab rechallenge in a *RAS* and *BRAF* wild type selected population[6]. This strategy was confirmed to be effective and despite the small sample size, clinical outcome was consistent with the findings of phase II studies. Moreover, we observed that in addition to the molecular selection through ctDNA analysis for *RAS-BRAF*, long anti-*EGFR* free interval was a prospective selection criterion for this therapeutic option. Thus, the combination of ctDNA analysis plus clinical elements might be a winning strategy overcoming the limitations of a single tool.

As for pancreatic cancer, the identification of prognostic and predictive biomarkers is an urgent medical need. Unfortunately, despite extensive research no robust validated factors to guide treatment choice are available, except for *BRCA* status, and no effective agents have drastically improved the management of this disease, including immunotherapy[7-10]. For this reason, we strongly agree with the authors that ctDNA detection appears as an appealing instrument to guide therapeutic choices across different treatment lines, in order to improve clinical outcomes pancreatic cancer patients. Indeed, liquid biopsy has shown to be more sensitive than carbohydrate antigen199 levels in predicting prognosis and treatment response[11].

Moreover, ctDNA evaluation has been shown to be more sensitive than current gold standard radiological methods (computed tomography) in the evaluation of the tumor burden at staging (for any micro dissemination or lymph node involvement) and for relapses detection[12-13].

At the present time, data regard small groups of patients and require validation in larger trials.

In conclusion, ctDNA qualifies as a promising main actor in the precision medicine era, with potential applications in the whole management of gastrointestinal cancer patients. Further larger and prospective studies are needed to assess the real impact of liquid biopsy in clinical practice, but for now, potential benefits are likely to overcome its limitations.

FOOTNOTES

Author contributions: Pretta A, Lai E, Donisi C, Spanu D, Ziranu P, Pusceddu V, Puzzoni M, Massa E, and Scartozzi M wrote and edited the manuscript.

Conflict-of-interest statement: Eleonora Lai has received advisory board and consultant fees from AstraZeneca and MSD. Mario Scartozzi has received consultant, advisory board and speakers' bureau fees from Amgen, Sanofi, MSD, EISAI, Merck, Bayer.

Country/Territory of origin: Italy

ORCID number: Andrea Pretta 0000-0002-0262-9270; Eleonora Lai 0000-0002-0275-8187; Clelia Donisi 0000-0003-4129-3375; Dario Spanu 0000-0003-2968-6811; Pina Ziranu 0000-0002-5659-7366; Valeria Pusceddu 0000-0003-4167-9091; Marco Puzzoni 0000-0001-5880-4309; Elena Massa 0000-0003-2018-5666; Mario Scartozzi 0000-0001-5977-5546.

S-Editor: Liu GL
L-Editor: A
P-Editor: Liu GL

REFERENCES

1 **Kirchweger P**, Wundsam HV, Rumpold H. Circulating tumor DNA for diagnosis, prognosis and treatment of gastrointestinal malignancies. *World J Clin Oncol* 2022; **13**: 473-484 [PMID: 35949436 DOI: 10.5306/wjco.v13.i6.473]
2 **Puzzoni M**, Ziranu P, Demurtas L, Lai E, Mariani S, Liscia N, Soro P, Pretta A, Impera V, Camera S, Musio F, Persano M, Donisi C, Tolu S, Balconi F, Scartozzi M. Why precision medicine should be applied across the continuum of care for metastatic colorectal cancer patients. *Future Oncol* 2020; **16**: 4337-4339 [PMID: 31793396 DOI: 10.2217/fon-2019-0624]
3 **Bregni G**, Pretta A, Senti C, Acedo Reina E, Vandeputte C, Trevisi E, Gkolfakis P, Kehagias P, Deleporte A, Van Laethem JL, Vergauwe P, Van den Eynde M, Deboever G, Janssens J, Demolin G, Holbrechts S, Clausse M, De Grez T, Peeters M, D'Hondt L, Geboes K, Besse-Hammer T, Rothé F, Flamen P, Hendlisz A, Sclafani F. Circulating DNA in the neoadjuvant setting of early stage colon cancer. *Acta Oncol* 2022; 1-7 [PMID: 35866544 DOI: 10.1080/0284186X.2022.2101023]
4 **Hendlisz A**, Golfinopoulos V, Deleporte A, Paesmans M, Mansy HE, Garcia C, Peeters M, Annemans L, Vandeputte C, Maetens M, Borbath I, Dresse D, Houbiers G, Fried M, Awada A, Piccart M, Laethem JL, Flamen P. Preoperative chemosensitivity testing as Predictor of Treatment benefit in Adjuvant stage III colon cancer (PePiTA): protocol of a prospective BGDO (Belgian Group for Digestive Oncology) multicentric study. *BMC Cancer* 2013; **13**: 190 [PMID: 23587148 DOI: 10.1186/1471-2407-13-190]
5 **Lai E**, Liscia N, Donisi C, Mariani S, Tolu S, Pretta A, Persano M, Pinna G, Balconi F, Pireddu A, Impera V, Dubois M, Migliari M, Spanu D, Saba G, Camera S, Musio F, Ziranu P, Puzzoni M, Demurtas L, Pusceddu V, Dettori M, Massa E, Atzori F, Dessì M, Astara G, Madeddu C, Scartozzi M. Molecular-Biology-Driven Treatment for Metastatic Colorectal Cancer. *Cancers (Basel)* 2020; **12** [PMID: 32413973 DOI: 10.3390/cancers12051214]
6 **Mariani S**, Puzzoni M, Giampieri R, Ziranu P, Pusceddu V, Donisi C, Persano M, Pinna G, Cimbro E, Parrino A, Spanu D, Pretta A, Lai E, Liscia N, Lupi A, Giglio E, Palomba G, Casula M, Pisano M, Palmieri G, Scartozzi M. Liquid Biopsy-Driven Cetuximab Rechallenge Strategy in Molecularly Selected Metastatic Colorectal Cancer Patients. *Front Oncol* 2022; **12**: 852583 [PMID: 35530345 DOI: 10.3389/fonc.2022.852583]
7 **Lai E**, Puzzoni M, Ziranu P, Pretta A, Impera V, Mariani S, Liscia N, Soro P, Musio F, Persano M, Donisi C, Tolu S, Balconi F, Pireddu A, Demurtas L, Pusceddu V, Camera S, Sclafani F, Scartozzi M. New therapeutic targets in pancreatic cancer. *Cancer Treat Rev* 2019; **81**: 101926 [PMID: 31739115 DOI: 10.1016/j.ctrv.2019.101926]
8 **Pretta A**, Lai E, Persano M, Donisi C, Pinna G, Cimbro E, Parrino A, Spanu D, Mariani S, Liscia N, Dubois M, Migliari M, Impera V, Saba G, Pusceddu V, Puzzoni M, Ziranu P, Scartozzi M. Uncovering key targets of success for immunotherapy in pancreatic cancer. *Expert Opin Ther Targets* 2021; **25**: 987-1005 [PMID: 34806517 DOI: 10.1080/14728222.2021.2010044]
9 **Golan T**, Hammel P, Reni M, Van Cutsem E, Macarulla T, Hall MJ, Park JO, Hochhauser D, Arnold D, Oh DY, Reinacher-Schick A, Tortora G, Algül H, O'Reilly EM, McGuinness D, Cui KY, Schlienger K, Locker GY, Kindler HL. Maintenance Olaparib for Germline *BRCA*-Mutated Metastatic Pancreatic Cancer. *N Engl J Med* 2019; **381**: 317-327 [PMID: 31157963 DOI: 10.1056/NEJMoa1903387]
10 **Lai E**, Ziranu P, Spanu D, Dubois M, Pretta A, Tolu S, Camera S, Liscia N, Mariani S, Persano M, Migliari M, Donisi C, Demurtas L, Pusceddu V, Puzzoni M, Scartozzi M. BRCA-mutant pancreatic ductal adenocarcinoma. *Br J Cancer* 2021; **125**: 1321-1332 [PMID: 34262146 DOI: 10.1038/s41416-021-01469-9]
11 **Kruger S**, Heinemann V, Ross C, Diehl F, Nagel D, Ormanns S, Liebmann S, Prinz-Bravin I, Westphalen CB, Haas M, Jung A, Kirchner T, von Bergwelt-Baildon M, Boeck S, Holdenrieder S. Repeated mutKRAS ctDNA measurements represent a novel and promising tool for early response prediction and therapy monitoring in advanced pancreatic cancer.

Ann Oncol 2018; **29**: 2348-2355 [PMID: 30346475 DOI: 10.1093/annonc/mdy417]

12 **Kirchweger P**, Kupferthaler A, Burghofer J, Webersinke G, Jukic E, Schwendinger S, Weitzendorfer M, Petzer A, Függer R, Rumpold H, Wundsam H. Circulating tumor DNA correlates with tumor burden and predicts outcome in pancreatic cancer irrespective of tumor stage. *Eur J Surg Oncol* 2022; **48**: 1046-1053 [PMID: 34876329 DOI: 10.1016/j.ejso.2021.11.138]

13 **Kirchweger P**, Kupferthaler A, Burghofer J, Webersinke G, Jukic E, Schwendinger S, Wundsam H, Biebl M, Petzer A, Rumpold H. Prediction of response to systemic treatment by kinetics of circulating tumor DNA in metastatic pancreatic cancer. *Front Oncol* 2022; **12**: 902177 [PMID: 36110940 DOI: 10.3389/fonc.2022.902177]

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