ISSN 1948-5204 (online)

World Journal of *Gastrointestinal Oncology*

Monthly Volume 17 Number 4 April 15, 2025

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Oncology

Contents

Monthly Volume 17 Number 4 April 15, 2025

EDITORIAL

REVIEW

ORIGINAL ARTICLE

Case Control Study

Retrospective Cohort Study

Retrospective Study

Clinical Trials Study

Observational Study

Prospective Study

Basic Study

ABOUT COVER

Peer Review of *World Journal of Gastrointestinal Oncology*, Jihwan Ko, MD, FRSPH, Director, Baekyang Jeil Internal Medicine Clinic, Busan 47181, South Korea. jihwanko65@gmail.com

AIMS AND SCOPE

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

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

INDEXING/ABSTRACTING

The *WJGO* is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJGO* as 2.5; JIF without journal self cites: 2.5; 5-year JIF: 2.8; JIF Rank: 72/143 in gastroenterology and hepatology; JIF Quartile: Q3; and 5-year JIF Quartile: Q2. The *WJGO*'s CiteScore for 2023 is 4.2 and Scopus CiteScore rank 2023: Gastroenterology is 80/167; Oncology is 196/404.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Monjur Ahmed

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5204/editorialboard.htm

PUBLICATION DATE
April 15, 2025

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 Gastrointestinal Oncology

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

World J Gastrointest Oncol 2025 April 15; 17(4): 102831

DOI: 10.4251/wjgo.v17.i4.102831

ISSN 1948-5204 (online)

EDITORIAL

Potential biomarkers for the prognosis of gastrointestinal stromal tumors

Yue-Fang Sun, Xuan-Ke Cao, Qing Wei, Yao-Hui Gao

Specialty type: Oncology

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

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade A, Grade B, Grade B

Novelty: Grade A, Grade B, Grade B

Creativity or Innovation: Grade A, Grade B, Grade C

Scientific Significance: Grade A, Grade B, Grade B

P-Reviewer: Khurram MF; Oprea V; Zhou YD

Received: November 6, 2024

Revised: January 17, 2025

Accepted: February 5, 2025

Published online: April 15, 2025

Processing time: 140 Days and 13.7 Hours

Yue-Fang Sun, Xuan-Ke Cao, Qing Wei, Yao-Hui Gao, Department of Pathology, Shanghai Tenth People's Hospital, Tongji University School of Medicine, Shanghai 200000, China

Co-first authors: Yue-Fang Sun and Xuan-Ke Cao.

Co-corresponding authors: Qing Wei and Yao-Hui Gao.

Corresponding author: Yao-Hui Gao, PhD, Professor, Department of Pathology, Shanghai Tenth People's Hospital, Tongji University School of Medicine, No. 301 Yanchang Middle Road, Shanghai 200000, China. gaoyaohui187@tongji.edu.cn

Abstract

In this editorial we comment on the article published in the recent issue of *World Journal of Gastrointestinal Oncology*. This study aims to explore the relationship between preoperative inflammation markers and the recurrence of gastrointestinal stromal tumors (GIST) after surgery. It is well known that the best-documented prognostic parameters for GIST are mitotic activity, tumor size and anatomical site. Besides, mutation status represents a prognostic as well as predictive factor. This study provides a new tool for postoperative recurrence risk assessment of GIST patients by establishing a line chart prediction model, which is certificated by previous research that high platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio correlated with increased tumour sizes, more advanced tumour stages and mitotic index. However, as a retrospective study, inevitable bias exists in the results; furthermore, the sample size of this study is relatively small, influencing the universality of the results. Moreover, when assessing risk rating and prognosis of GIST, some novel inflammatory makers could be taken into consideration, such as proenkephalin and SLITRK3. Overall, this study can offer an additional model for GIST prognosis and recurrence risk assessment, independent of the traditional prognostic factors of GIST.

Key Words: Gastrointestinal stromal tumors; Prognostic parameters; Inflammatory markers; Recurrence risk; Personalized therapy

Core Tip: The importance of predicting prognosis in the management of gastrointestinal stromal tumors (GIST) is well known, with a particular focus on mitotic activity, tumor size, anatomical location, and KIT and platelet-derived growth factor receptor alpha mutation status. It underscores the emerging significance of inflammatory markers such as the neutrophil-to-lymphocyte ratio, systemic immune-to-inflammation index, platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) in predicting GIST prognosis and recurrence risk. This study identified the MLR and PLR as independent risk factors, thereby providing a predictive model for recurrence-free survival. However, it is important to note that the study has limitations, including its retrospective design, small sample size, and lack of external validation.

Citation: Sun YF, Cao XK, Wei Q, Gao YH. Potential biomarkers for the prognosis of gastrointestinal stromal tumors. *World J Gastrointest Oncol* 2025; 17(4): 102831
URL: https://www.wjgnet.com/1948-5204/full/v17/i4/102831.htm
DOI: https://dx.doi.org/10.4251/wjgo.v17.i4.102831

INTRODUCTION

Gastrointestinal stromal tumors (GIST) are mesenchymal tumor with variable behavior, with an incidence ranging from 1.1 cases per 100000 person/years to 1.5 cases per 100000 person/years[1]. In contrast, microGIST are relatively common. Prognostic parameters play a crucial role in the management of GIST, helping to estimate the risk of recurrence after surgery, which is essential for establishing adjuvant therapy schemes. The best-documented prognostic parameters for GIST are mitotic activity, tumor size and anatomical site. Besides, mutation status of KIT and platelet-derived growth factor receptor alpha serves as a prognostic and predictive parameter[2,3]. These elements are incorporated into the National Institutes of Health risk classification system, which categorizes GIST cases into low-risk, intermediate-risk, and high-risk groups for recurrence[4,5]. This classification facilitates establish the strategy of adjuvant therapy, highlighting the importance of prognostic indicators. It is recommended that patients with high-risk GSIT may get privileged form a standard three-years adjuvant treatment. Many clinical trials have recommended imatinib as the first-line treatment for GIST, with sunitinib, regorafenib, and ripretinib identified as subsequent therapeutic options for advanced cases[3]. Additionally, various tyrosine kinase inhibitors are utilized in different treatment settings[6].

EXPANDING INFLAMMATORY INDICATORS FOR GIST

In recent years, inflammatory markers, such as the neutrophil-to-lymphocyte ratio, systemic immune-to-inflammation index, platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), have demonstrated potential value for the prognosis of various cancers, including GIST[7-10]. Compared with classical prognostic parameters, inflammatory markers are readily accessible and cost effective to examine, and they provide additional prognostic information that allows clinicians to conduct more comprehensive assessments[8,9]. In patients with GIST, inflammatory markers are associated with the risk of disease recurrence. These markers not only reflect the systemic antitumour inflammatory response but are also closely associated with tumour progression, invasion, and prognosis. Elevated levels of certain markers may indicate a more aggressive disease phenotype and poorer prognosis in patients with GIST. Additionally, inflammatory markers have also been explored for their ability to predict neoadjuvant and immunotherapy efficacy in advanced tumour patients[11,12]. Additionally, in GIST, inflammatory markers are related to angiogenesis and the immune response within the tumour microenvironment. These markers provide insights into the host immune status, which can be useful for making personalized treatment decisions. Furthermore, certain inflammatory markers may serve as predictors of adjuvant treatment efficacy, indicating promising prognostic value for recurrence-free survival (RFS) in patients (Table 1)[3,13-21].

However, these results may be influenced by various factors, including infection status, nutritional status, and other conditions unrelated to cancer. This could result in false-positive outcomes during prognostic assessments. Therefore, ensuring the consistency and reproducibility of inflammatory markers is essential for their clinical application. Further validation of their prognostic value calls for larger, multicenter studies. Standardized thresholds should be established for these markers[3,14]. It is highly important to establish standardized thresholds and interpretations for these markers to increase their reliability across different studies and clinical settings.

In this study, which identified the MLR and PLR as independent risk factors among four inflammatory biomarkers derived from neutrophils, platelets, monocytes, and lymphocytes (Figure 1), the authors established a line chart prediction model correlating inflammatory markers with RFS and offered a novel clinical tool for assessing postoperative recurrence risk in GIST patients. This study also emphasized the ongoing sensitivity of inflammatory markers in patients receiving postoperative targeted therapy.

Nevertheless, as a relatively small-sample retrospective study, there was inevitable bias in the results. Second, the study only conducted internal validation without external or multicenter data verification. Third, the impact of postoperative targeted therapy on prognostic data may not fully reflect the operative situation. A larger sample size, external validation of the prediction model, deeper exploration of novel biomarkers, better handling of confounding factors, and improved practical application of findings for this study are highly important. We suggest that future studies create a

Table 1 Relationship between systemic inflammatory markers and the prognosis of gastrointestinal stromal tumors

Inflammatory markers	Impact	Mechanism	Threshold value	Ref.
NLR	High preoperative NLR is associated with decreased DFS and is an independent prognostic factor	Higher NLR may reflect the inflammatory state and immunosuppressive state of the body, which may be related to tumor progression and response to treatment	1.92-6	Kumarasamy *et al* [14], Bigot *et al* [20], Malietzis *et al* [21]
SII	A promising predictor for RFS and effect of neoadjuvant therapy	A high level of SII indicates an enhanced systemic inflammatory state and a weakened immune response, while a high level of SII may indicate that the inflammatory microenvironment promotes tumor invasion and metastasis	544.6-820.0	Goh *et al*[16], Lu *et al*[17]
PLR	High PLR is an independent prognostic factor for RFS in patients with GIST	High PLR may indicate the immune surveillance ability is decreased, which may be related to tumor progression	275	
PENK	High expression of PENK was associated with superior OS and RFS in patients with GIST	PENK is a neuropeptide precursor, which may affect the proliferation and apoptosis of tumor cells through its interaction with opioid receptors. The high expression of PENK may be related to the tumor inhibition pathway	IHC score ≥ 4: PENK positive. IHC score < 4: PENK negative	
GNRI	A promising predictor for RFS	GNRI is an objective nutritional assessment method based on serum albumin levels and body weight ratios, reflecting the nutritional status of patients to influence prognosis	98.3	Lu *et al*[17]
PNI	A promising predictor for effect of neoadjuvant therapy	PNI reflects the nutritional status and immune function of patients. Low PNI may indicate decreased immune function and poor nutritional status, further promoting the formation of an inflammatory microenvironment	47.2	
MLR	As a prognostic indicator for the recurrence of GIST, with elevated MLR correlating with an increased risk of postoperative recurrence	Monocytes and lymphocytes play crucial roles in the immune modulation within the tumor microenvironment. A high MLR may signify underlying chronic inflammation, which could facilitate tumor progression and recurrence. Furthermore, an elevated MLR might reflect compromised immune surveillance capabilities	/	
SLITRK3	SLITRK3 expression is closely associated with OS and DFS in GIST patients	Elevated levels of SLITRK3 may be linked to the aggressiveness and unfavorable prognosis of GIST; however, the precise mechanisms underlying its action and the critical pathways involved in GIST remain to be elucidated	IHC score ≥ 4: SLITRK3 positive. IHC score < 4: SLITRK3 negative	

DFS: Disease-free survival; GNRI: Geriatric nutritional risk index; IHC: Immunohistochemical; MLR: Monocyte-to-lymphocyte ratio; NLR: Neutrophil-to-lymphocyte ratio; OS: Overall survival; PENK: Proenkephalin; PLR: Platelet-to-lymphocyte ratio; PNI: Prognostic nutritional index; RFS: Recurrence-free survival; SII: Systemic immune-to-inflammation index.

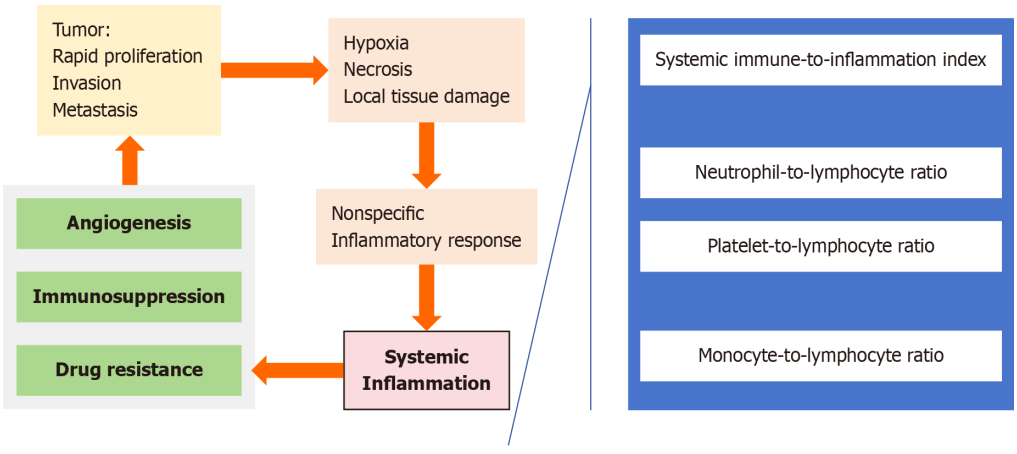

Figure 1 The effect of four inflammatory biomarkers derived from neutrophils, platelets, monocytes, and lymphocytes.

user-friendly online platform where clinicians can input patient data, obtain prognostic predictions on the basis of the model and validate standardized thresholds for the inflammatory markers used in the model.

NOVEL PROGNOSTIC PARAMETERS FOR GIST

Research into novel prognostic parameters for GIST is thriving. New markers such as cytokines and chemokines are being explored for their potential role in GIST prognosis. Recent studies identified SLITRK3 as a significant predictor for the recurrence and metastasis of GIST, with higher expression levels correlating with poorer patient outcomes[18]. On the other hand, another study found that high proenkephalin (PENK) expression in GIST is associated with better overall survival and RFS[19]. On the molecular front, next-generation sequencing of liquid biopsy detecting circulating tumor DNA offers a non-invasive approach to detect mutation status and monitor progression and response to treatment in real-time[22].

CONCLUSION

In conclusion, integration both classical and novel prognostic parameters-including inflammatory markers-into the clinical management of GIST, is essential for personalized treatment strategies. These markers hold promising value for enhancing risk stratification, guiding adjuvant therapy decisions, and improving our ability to predict and manage disease recurrence among GIST patients. Further research is warranted to fully elucidate the mechanisms underlying the association between inflammation and GIST progression and to translate these findings into clinical practice.

FOOTNOTES

Author contributions: Sun YF, Cao XK, Wei Q and Gao YH designed and performed the research study; all of the authors read and approved the final version of the manuscript to be published.

Conflict-of-interest statement: All authors declare no conflict of interest in publishing the manuscript.

Country of origin: China

ORCID number: Yao-Hui Gao 0000-0002-6830-5295.

S-Editor: Luo ML
L-Editor: A
P-Editor: Wang WB

REFERENCES

1 **Nilsson B**, Bümming P, Meis-Kindblom JM, Odén A, Dortok A, Gustavsson B, Sablinska K, Kindblom LG. Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era--a population-based study in western Sweden. *Cancer* 2005; **103**: 821-829 [PMID: 15648083 DOI: 10.1002/cncr.20862]

2 **Joensuu H**, Vehtari A, Riihimäki J, Nishida T, Steigen SE, Brabec P, Plank L, Nilsson B, Cirilli C, Braconi C, Bordoni A, Magnusson MK, Linke Z, Sufliarsky J, Federico M, Jonasson JG, Dei Tos AP, Rutkowski P. Risk of recurrence of gastrointestinal stromal tumour after surgery: an analysis of pooled population-based cohorts. *Lancet Oncol* 2012; **13**: 265-274 [PMID: 22153892 DOI: 10.1016/S1470-2045(11)70299-6]

3 **Zhao JL**, Wang MY, Lv YZ, Zhou YJ. Prognostic value of inflammatory markers in predicting recurrence-free survival in gastrointestinal stromal tumor patients: A nomogram-based approach. *World J Gastrointest Oncol* 2024; **17**: 94956

4 **Miettinen M**, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. *Semin Diagn Pathol* 2006; **23**: 70-83 [PMID: 17193820 DOI: 10.1053/j.semdp.2006.09.001]

5 **Fletcher CD**, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, Miettinen M, O'Leary TJ, Remotti H, Rubin BP, Shmookler B, Sobin LH, Weiss SW. Diagnosis of gastrointestinal stromal tumors: A consensus approach. *Hum Pathol* 2002; **33**: 459-465 [PMID: 12094370 DOI: 10.1053/hupa.2002.123545]

6 **van de Wal D**, Elie M, Le Cesne A, Fumagalli E, den Hollander D, Jones RL, Marquina G, Steeghs N, van der Graaf WTA, Husson O. Health-Related Quality of Life and Side Effects in Gastrointestinal Stromal Tumor (GIST) Patients Treated with Tyrosine Kinase Inhibitors: A Systematic Review of the Literature. *Cancers (Basel)* 2022; **14**: 1832 [PMID: 35406604 DOI: 10.3390/cancers14071832]

7 **Huang H**, Liu Q, Zhu L, Zhang Y, Lu X, Wu Y, Liu L. Prognostic Value of Preoperative Systemic Immune-Inflammation Index in Patients with Cervical Cancer. *Sci Rep* 2019; **9**: 3284 [PMID: 30824727 DOI: 10.1038/s41598-019-39150-0]

8 **Yilmaz A**, Mirili C, Bilici M, Tekin SB. A novel predictor in patients with gastrointestinal stromal tumors: Systemic immune-inflammation index (SII). *J BUON* 2019; **24**: 2127-2135 [PMID: 31786885]

9 **Yang J**, Gu Y, Huang X, Xu J, Zhang Y, Yang X, Tian H, Zhan W. Prognostic impact of preoperative neutrophil-lymphocyte ratio for surgically resected gastrointestinal stromal tumors. *Medicine (Baltimore)* 2019; **98**: e15319 [PMID: 31008985 DOI: 10.1097/MD.0000000000015319]

10 **Wei ZW**, Huang WB, Yang DJ, Yuan YJ, He YL, Zhang CH. The prognostic roles of platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio in gastrointestinal stromal tumours: a meta-analysis. *Transl Cancer Res* 2020; **9**: 5128-5138 [PMID: 35117879 DOI: 10.21037/tcr-20-1037]

11 **Zheng F**, Meng Q, Zhang L, Chen J, Zhao L, Zhou Z, Liu Y. Prognostic roles of hematological indicators for the efficacy and prognosis of immune checkpoint inhibitors in patients with advanced tumors: a retrospective cohort study. *World J Surg Oncol* 2023; **21**: 198 [PMID: 37420219 DOI: 10.1186/s12957-023-03077-8]

12 **Ding P**, Wu J, Wu H, Sun C, Guo H, Lowe S, Yang P, Tian Y, Liu Y, Meng L, Zhao Q. Inflammation and nutritional status indicators as prognostic indicators for patients with locally advanced gastrointestinal stromal tumors treated with neoadjuvant imatinib. *BMC Gastroenterol* 2023; **23**: 23 [PMID: 36690935 DOI: 10.1186/s12876-023-02658-x]

13 **Cananzi FCM**, Minerva EM, Samà L, Ruspi L, Sicoli F, Conti L, Fumagalli Romario U, Quagliuolo VL. Preoperative monocyte-to-lymphocyte ratio predicts recurrence in gastrointestinal stromal tumors. *J Surg Oncol* 2019; **119**: 12-20 [PMID: 30426498 DOI: 10.1002/jso.25290]

14 **Kumarasamy C**, Tiwary V, Sunil K, Suresh D, Shetty S, Muthukaliannan GK, Baxi S, Jayaraj R. Prognostic Utility of Platelet-Lymphocyte Ratio, Neutrophil-Lymphocyte Ratio and Monocyte-Lymphocyte Ratio in Head and Neck Cancers: A Detailed PRISMA Compliant Systematic Review and Meta-Analysis. *Cancers (Basel)* 2021; **13**: 4166 [PMID: 34439320 DOI: 10.3390/cancers13164166]

15 **Luo XF**, Zhou LH. Prognostic significance of neutrophil to lymphocyte ratio in patients with gastrointestinal stromal tumors: A meta-analysis. *Clin Chim Acta* 2018; **477**: 7-12 [PMID: 29175648 DOI: 10.1016/j.cca.2017.11.029]

16 **Goh BK**, Chok AY, Allen JC Jr, Quek R, Teo MC, Chow PK, Chung AY, Ong HS, Wong WK. Blood neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios are independent prognostic factors for surgically resected gastrointestinal stromal tumors. *Surgery* 2016; **159**: 1146-1156 [PMID: 26688506 DOI: 10.1016/j.surg.2015.10.021]

17 **Lu Z**, Li R, Cao X, Liu C, Sun Z, Shi X, Shao W, Zheng Y, Song J. Assessment of Systemic Inflammation and Nutritional Indicators in Predicting Recurrence-Free Survival After Surgical Resection of Gastrointestinal Stromal Tumors. *Front Oncol* 2021; **11**: 710191 [PMID: 34381731 DOI: 10.3389/fonc.2021.710191]

18 **Wang CJ**, Zhang ZZ, Xu J, Wang M, Zhao WY, Tu L, Zhuang C, Liu Q, Shen YY, Cao H, Zhang ZG. SLITRK3 expression correlation to gastrointestinal stromal tumor risk rating and prognosis. *World J Gastroenterol* 2015; **21**: 8398-8407 [PMID: 26217092 DOI: 10.3748/wjg.v21.i27.8398]

19 **Tang D**, Lin T, Wang Y, Cao H. High expression of proenkephalin is associated with favorable outcomes in patients with gastrointestinal stromal tumors. *Cancer Manag Res* 2019; **11**: 6681-6690 [PMID: 31410059 DOI: 10.2147/CMAR.S202044]

20 **Bigot F**, Castanon E, Baldini C, Hollebecque A, Carmona A, Postel-Vinay S, Angevin E, Armand JP, Ribrag V, Aspeslagh S, Varga A, Bahleda R, Menis J, Gazzah A, Michot JM, Marabelle A, Soria JC, Massard C. Prospective validation of a prognostic score for patients in immunotherapy phase I trials: The Gustave Roussy Immune Score (GRIm-Score). *Eur J Cancer* 2017; **84**: 212-218 [PMID: 28826074 DOI: 10.1016/j.ejca.2017.07.027]

21 **Malietzis G**, Giacometti M, Askari A, Nachiappan S, Kennedy RH, Faiz OD, Aziz O, Jenkins JT. A preoperative neutrophil to lymphocyte ratio of 3 predicts disease-free survival after curative elective colorectal cancer surgery. *Ann Surg* 2014; **260**: 287-292 [PMID: 24096764 DOI: 10.1097/SLA.0000000000000216]

22 **Calderillo-Ruíz G**, Pérez-Yepez EA, García-Gámez MA, Millan-Catalan O, Díaz-Romero C, Ugalde-Silva P, Salas-Benavides R, Pérez-Plasencia C, Carbajal-López B. Genomic profiling in GIST: Implications in clinical outcome and future challenges. *Neoplasia* 2024; **48**: 100959 [PMID: 38183711 DOI: 10.1016/j.neo.2023.100959]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com