

World Journal of *Clinical Oncology*

World J Clin Oncol 2024 January 24; 15(1): 1-164



Contents

Monthly Volume 15 Number 1 January 24, 2024

EDITORIAL

- 1 Re-evaluating the role of pelvic radiation in the age of modern precision medicine and systemic therapy
Ke TW, Liao YM, Chang SC, Lin CH, Chen WTL, Liang JA, Chien CR
- 5 Prognostic factors of breast cancer brain metastasis
Yakar M, Etiz D

REVIEW

- 9 Inflammatory response in gastrointestinal cancers: Overview of six transmembrane epithelial antigens of the prostate in pathophysiology and clinical implications
Fang ZX, Chen WJ, Wu Z, Hou YY, Lan YZ, Wu HT, Liu J

MINIREVIEWS

- 23 Uveal melanoma: Recent advances in immunotherapy
Sorrentino FS, De Rosa F, Di Terlizzi P, Toneatto G, Gabai A, Finocchio L, Salati C, Spadea L, Zeppieri M

ORIGINAL ARTICLE

Clinical and Translational Research

- 32 Scinderin promotes glioma cell migration and invasion *via* remodeling actin cytoskeleton
Lin X, Zhao Z, Sun SP, Liu W
- 45 Prognostic and immunological roles of heat shock protein A4 in lung adenocarcinoma
Wu X, Yang SY, Zhang YH, Fang JZ, Wang S, Xu ZW, Zhang XJ
- 62 Identification of the key genes and mechanisms associated with transcatheter arterial chemoembolisation refractoriness in hepatocellular carcinoma
Huang JZ, Li JD, Chen G, He RQ
- 89 Predicting colorectal cancer prognosis based on long noncoding RNAs of disulfidptosis genes
Wang KL, Chen KD, Tang WW, Chen ZP, Wang YJ, Shi GP, Chen YG
- 115 Gene signatures to therapeutics: Assessing the potential of ivermectin against t(4;14) multiple myeloma
Song Y, Zhang HJ, Song X, Geng J, Li HY, Zhang LZ, Yang B, Lu XC

Basic Study

- 130 Fatty acid binding protein 5 is a novel therapeutic target for hepatocellular carcinoma
Li Y, Lee W, Zhao ZG, Liu Y, Cui H, Wang HY

SCIENTOMETRICS

- 145** What are the changes in the hotspots and frontiers of microRNAs in hepatocellular carcinoma over the past decade?

Zhang L, Chen ZY, Wei XX, Li JD, Chen G

CASE REPORT

- 159** Radiotherapy for hyoid bone metastasis from lung adenocarcinoma: A case report

Hsu J, Hribar K, Poen J

ABOUT COVER

Peer Reviewer of *World Journal of Clinical Oncology*, Hui-Xia Lu, PhD, Professor, Department of Gynecology and Obstetrics, Clinical Medical College, University of Dali, Dali 671003, Yunnan Province, China.
haohao021021@foxmail.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 Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for WJCO as 2.8; IF without journal self cites: 2.8; 5-year IF: 3.0; Journal Citation Indicator: 0.36.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Xiang-Di Zhang; Production Department Director: Xu Guo; Editorial Office Director: Xu Guo.

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.wjnet.com/2218-4333/editorialboard.htm>

PUBLICATION DATE

January 24, 2024

COPYRIGHT

© 2024 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Re-evaluating the role of pelvic radiation in the age of modern precision medicine and systemic therapy

Tao-Wei Ke, Yu-Min Liao, Sheng-Chi Chang, Che-Hung Lin, William Tzu-Liang Chen, Ji-An Liang, Chun-Ru Chien

Specialty type: Oncology

Provenance and peer review:

Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

P-Reviewer: Chen N, China; Yakar M, Turkey

Received: September 25, 2023

Peer-review started: September 25, 2023

First decision: December 2, 2023

Revised: December 9, 2023

Accepted: December 29, 2023

Article in press: December 29, 2023

Published online: January 24, 2024



Tao-Wei Ke, Sheng-Chi Chang, William Tzu-Liang Chen, Department of Colorectal Surgery, China Medical University Hospital, Taichung 40402, Taiwan

Tao-Wei Ke, School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung 40402, Taiwan

Yu-Min Liao, Che-Hung Lin, Division of Hematology and Oncology, Department of Internal Medicine, China Medical University Hospital, Taichung 40402, Taiwan

William Tzu-Liang Chen, Department of Colorectal Surgery, China Medical University Hsinchu Hospital, Hsinchu 30272, Taiwan

William Tzu-Liang Chen, Ji-An Liang, School of Medicine, College of Medicine, China Medical University, Taichung 40402, Taiwan

Ji-An Liang, Chun-Ru Chien, Department of Radiation Oncology, China Medical University Hospital, Taichung 40402, Taiwan

Corresponding author: Chun-Ru Chien, MD, PhD, Doctor, Professor, Department of Radiation Oncology, China Medical University Hospital, No. 91 Hsueh-Shih Road, North District, Taichung 40402, Taiwan. d16181@gmail.com

Abstract

The efficacy of pelvic radiation in the management of locally advanced stage rectal cancer has come under scrutiny in the context of modern precision medicine and systemic therapy as evidenced by recent clinical trials such as FOWARC (*J Clin Oncol* 2019; 37: 3223-3233), NCT04165772 (*N Engl J Med* 2022; 386: 2363-2376), and PROSPECT (*N Engl J Med* 2023; 389: 322-334). In this review, we comprehensively assess these pivotal trials and offer additional insights into the evolving role of pelvic radiation in contemporary oncology.

Key Words: Radiotherapy; Locally advanced stage rectal cancer; Precision medicine; Systemic therapy; Clinical trial

©The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Neoadjuvant systemic therapy alone without radiation represents a viable option for locally advanced rectal cancer patients, particularly when organ preservation is not a priority. Nevertheless, it is crucial to engage in multidisciplinary discussions, especially considering the limited long-term experience.

Citation: Ke TW, Liao YM, Chang SC, Lin CH, Chen WTL, Liang JA, Chien CR. Re-evaluating the role of pelvic radiation in the age of modern precision medicine and systemic therapy. *World J Clin Oncol* 2024; 15(1): 1-4

URL: <https://www.wjgnet.com/2218-4333/full/v15/i1/1.htm>

DOI: <https://dx.doi.org/10.5306/wjco.v15.i1.1>

INTRODUCTION

Pelvic radiation has traditionally played an essential role in neoadjuvant therapy for locally advanced rectal cancer (LARC) in the past, either as neoadjuvant concurrent chemoradiotherapy (nCCRT) or neoadjuvant short course radiotherapy (nSCRT)[1-3]. However, its efficacy has come under scrutiny in the context of modern precision medicine and systemic therapy as evidenced by recent clinical trials[4-6] and a systematic review[7]. Consequently, the use of neoadjuvant systemic therapy alone without radiation has emerged as one of the alternatives in contemporary guidelines for patients with certain genetic mutations who achieved a complete clinical response after immunotherapy or patients with a good response (> 20%) after chemotherapy[8]. In addition, patients with high-risk features such as threatened mesorectal fascia, N2 stage, or extramural vascular invasion were not good candidates for the use of chemotherapy without radiation[6,8].

MAIN BODY

In this editorial, we have summarized select relevant trials in Table 1[4-6,9,10], which provide the rationale for employing neoadjuvant systemic therapy alone without radiation in specific LARC cases. However, we would like to highlight two additional considerations regarding the omission of pelvic radiation for LARC.

Table 1 Key characteristic of trials investigating neoadjuvant systemic therapy alone without radiation in locally advanced rectal cancer									
Study	ID	Design	LARC	Study group	Comparator group(s)	mFU	pCR (%)	Local control (%)	OS (%)
FOWARC[4]	NCT01211210	Phase 3	Suitable for curative resection	FOLFOX	CCRT	45.2	6.5 vs (14 or 27.5); <i>P</i> = 0.05	3-year LRR 8.3 vs (8 or 7); <i>P</i> = 0.873	3-year 90.7 vs (91.3 or 89.1); <i>P</i> = 0.971
PROSPECT [6]	NCT01515787	Phase 3	T2N1, T3N0, T3N1	FOLFOX	CCRT	58	21.9 vs 24.3; <i>P</i> value NA	5-year LR 1.8% vs 1.6%; <i>P</i> value > 0.05	5-year 89.5 vs 90.2; <i>P</i> value > 0.05
GRECCAR4 [9]	NCT01333709	Phase 2 RCT	T3d with predictive CRM 1 mm	FOLFIRINOX	CCRT	65.7	(10 or 13.5) vs (58 or 20); <i>P</i> value NA	NA	5-year (90 or 84.3) vs (93.3 or 86.1); <i>P</i> value > 0.05
CONVERT [10]	NCT02288195	Phase 3	cT2N+ or cT3-4Nany uninvolved mesorectal fascia	CAPOX	CCRT	NA	11 vs 13.8; <i>P</i> = 0.33	NA	NA
19-288[5]	NCT04165772	Phase 2	Mismatch repair-deficient	Dostarlimab	NA	NA	NA	100	100

LARC: Locally advanced rectal cancer; LR: Local recurrence; LRR: Locoregional recurrence; mFU: Median follow up (in months); pCR: Pathological complete response; OS: Overall survival; CCRT: Concurrent chemoradiotherapy; CRM: Circumferential resection margin; NA: Not available; RCT: Randomized controlled trial.

First, it is imperative to await long-term follow-up results from the aforementioned studies. For instance, the initial publication of the RAPIDO trial reported no statistically significant difference in locoregional failure between nSCRT followed by chemotherapy and nCCRT (*P* = 0.12)[11]. However, the disparity in locoregional failure became more pronounced with borderline statistical significance after extended follow-up (*P* = 0.07)[12]. This finding has led to nSCRT being less favored by certain experts[13] and in the current guidelines[8]. It is worth noting that the biological equivalent dose in radiotherapy of nCCRT is higher than that of nSCRT [EQD2(10) 50 Gy vs 37.5 Gy][14].

Second, one of the potential objectives in modern LARC management is organ preservation, for which nCCRT in the context of total neoadjuvant therapy has shown great promise[15,16]. Therefore, when sphincter or organ preservation is the goal, concerns may arise about the suitability of neoadjuvant systemic therapy alone without radiation[13].

CONCLUSION

In summary, neoadjuvant systemic therapy alone without radiation represents a viable option for LARC patients, particularly when organ preservation is not a priority. Nevertheless, it is crucial to engage in multidisciplinary discussions, especially considering the limited long-term experience. We eagerly anticipate the results of ongoing trials, such as NCT04495088 and NCT04749108, which will provide further insights into this evolving treatment approach.

FOOTNOTES

Co-first authors: Tao-Wei Ke and Yu-Min Liao.

Author contributions: Ke TW and Liao YM contributed equally to this work; Ke TW, Liao YM, Chang SC, Chen WTL, Liang JA, and Chien CR made substantial contribution to the design of the work, to the interpretation of data, and to revise the manuscript; all have read and approve the final manuscript. The choice of these researchers (Ke TW and Liao YM) as co-first authors acknowledges and respects this equal contribution, while recognizing the spirit of teamwork and collaboration of this study. In summary, we believe that designating Ke TW and Liao YM as co-first authors is fitting for our manuscript as it accurately reflects our team's collaborative spirit, equal contributions, and diversity.

Supported by National Science and Technology Council, No. NSTC 112-2314-B-039-048.

Conflict-of-interest statement: We declared no conflict 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/>

Country/Territory of origin: Taiwan

ORCID number: Chun-Ru Chien 0000-0002-2365-7641.

S-Editor: Lin C

L-Editor: A

P-Editor: Zhang XD

REFERENCES

- 1 Sauer R, Becker H, Hohenberger W, Rödel C, Wittekind C, Fietkau R, Martus P, Tschmelitsch J, Hager E, Hess CF, Karstens JH, Liersch T, Schmidberger H, Raab R; German Rectal Cancer Study Group. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med* 2004; **351**: 1731-1740 [PMID: 15496622 DOI: 10.1056/NEJMoa040694]
- 2 Kapiteijn E, Marijnen CA, Nagtegaal ID, Putter H, Steup WH, Wiggers T, Rutten HJ, Pahlman L, Glimelius B, van Krieken JH, Leer JW, van de Velde CJ; Dutch Colorectal Cancer Group. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med* 2001; **345**: 638-646 [PMID: 11547717 DOI: 10.1056/NEJMoa010580]
- 3 Koukourakis GV. Role of radiation therapy in neoadjuvant era in patients with locally advanced rectal cancer. *World J Gastrointest Oncol* 2012; **4**: 230-237 [PMID: 23443049 DOI: 10.4251/wjgo.v4.i12.230]
- 4 Deng Y, Chi P, Lan P, Wang L, Chen W, Cui L, Chen D, Cao J, Wei H, Peng X, Huang Z, Cai G, Zhao R, Xu L, Zhou H, Wei Y, Zhang H, Zheng J, Huang Y, Zhou Z, Cai Y, Kang L, Huang M, Wu X, Peng J, Ren D, Wang J. Neoadjuvant Modified FOLFOX6 With or Without Radiation Versus Fluorouracil Plus Radiation for Locally Advanced Rectal Cancer: Final Results of the Chinese FOWARC Trial. *J Clin Oncol* 2019; **37**: 3223-3233 [PMID: 31557064 DOI: 10.1200/JCO.18.02309]
- 5 Cercek A, Lumish M, Sinopoli J, Weiss J, Shia J, Lamendola-Essel M, El Dika IH, Segal N, Shcherba M, Sugarman R, Stadler Z, Yaeger R, Smith JJ, Rousseau B, Argiles G, Patel M, Desai A, Saltz LB, Widmar M, Iyer K, Zhang J, Gianino N, Crane C, Romesser PB, Pappou EP, Paty P, Garcia-Aguilar J, Gonen M, Gollub M, Weiser MR, Schaller KA, Diaz LA Jr. PD-1 Blockade in Mismatch Repair-Deficient, Locally Advanced Rectal Cancer. *N Engl J Med* 2022; **386**: 2363-2376 [PMID: 35660797 DOI: 10.1056/NEJMoa2201445]
- 6 Schrag D, Shi Q, Weiser MR, Gollub MJ, Saltz LB, Musher BL, Goldberg J, Al Baghdadi T, Goodman KA, McWilliams RR, Farma JM, George TJ, Kennecke HF, Shergill A, Montemurro M, Nelson GD, Colgrove B, Gordon V, Venook AP, O'Reilly EM, Meyerhardt JA, Dueck AC, Basch E, Chang GJ, Mamon HJ. Preoperative Treatment of Locally Advanced Rectal Cancer. *N Engl J Med* 2023; **389**: 322-334 [PMID: 37272534 DOI: 10.1056/NEJMoa2303269]
- 7 Wu P, Xu HM, Zhu Z. Neoadjuvant chemotherapy without radiation as a potential alternative treatment for locally advanced rectal cancer: A meta-analysis. *World J Gastrointest Oncol* 2021; **13**: 1196-1209 [PMID: 34616523 DOI: 10.4251/wjgo.v13.i9.1196]

- 8 **National Comprehensive Cancer Network.** Guidelines for Rectal Cancers, version 6.2023. [cited 24 November 2022]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf
- 9 **Rouanet P,** Rullier E, Lelong B, Maingon P, Tuech JJ, Pezet D, Castan F, Nougaret S; GRECCAR Study Group*. Tailored Strategy for Locally Advanced Rectal Carcinoma (GRECCAR 4): Long-term Results From a Multicenter, Randomized, Open-Label, Phase II Trial. *Dis Colon Rectum* 2022; **65**: 986-995 [PMID: [34759247](#) DOI: [10.1097/DCR.0000000000002153](#)]
- 10 **Mei WJ,** Wang XZ, Li YF, Sun YM, Yang CK, Lin JZ, Wu ZG, Zhang R, Wang W, Li Y, Zhuang YZ, Lei J, Wan XB, Ren YK, Cheng Y, Li WL, Wang ZQ, Xu DB, Mo XW, Ju HX, Ye SW, Zhao JL, Zhang H, Gao YH, Zeng ZF, Xiao WW, Zhang XP, Zhang X, Xie E, Feng YF, Tang JH, Wu XJ, Chen G, Li LR, Lu ZH, Wan DS, Bei JX, Pan ZZ, Ding PR. Neoadjuvant Chemotherapy With CAPOX Versus Chemoradiation for Locally Advanced Rectal Cancer With Uninvolved Mesorectal Fascia (CONVERT): Initial Results of a Phase III Trial. *Ann Surg* 2023; **277**: 557-564 [PMID: [36538627](#) DOI: [10.1097/SLA.0000000000005780](#)]
- 11 **Bahadoer RR,** Dijkstra EA, van Etten B, Marijnen CAM, Putter H, Kranenbarg EM, Roodvoets AGH, Nagtegaal ID, Beets-Tan RGH, Blomqvist LK, Fokstuen T, Ten Tije AJ, Capdevila J, Hendriks MP, Edhemovic I, Cervantes A, Nilsson PJ, Glimelius B, van de Velde CJH, Hospers GAP; RAPIDO collaborative investigators. Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial. *Lancet Oncol* 2021; **22**: 29-42 [PMID: [33301740](#) DOI: [10.1016/S1470-2045\(20\)30555-6](#)]
- 12 **Dijkstra EA,** Nilsson PJ, Hospers GAP, Bahadoer RR, Meershoek-Klein Kranenbarg E, Roodvoets AGH, Putter H, Berglund Å, Cervantes A, Crolla RMPH, Hendriks MP, Capdevila J, Edhemovic I, Marijnen CAM, van de Velde CJH, Glimelius B, van Etten B; Collaborative Investigators. Locoregional Failure During and After Short-course Radiotherapy Followed by Chemotherapy and Surgery Compared With Long-course Chemoradiotherapy and Surgery: A 5-Year Follow-up of the RAPIDO Trial. *Ann Surg* 2023; **278**: e766-e772 [PMID: [36661037](#) DOI: [10.1097/SLA.0000000000005799](#)]
- 13 **Vailati BB,** Cerdán-Santacruz C, São Julião GP, Corbi L, Perez RO. Short-Course Radiation and Consolidation Chemotherapy for Rectal Cancer-The Rise and Fall of a Treatment Strategy-Rest in Peace. *Dis Colon Rectum* 2023; **66**: 1297-1299 [PMID: [37379161](#) DOI: [10.1097/DCR.0000000000002997](#)]
- 14 **Bentzen SM,** Dörr W, Gahbauer R, Howell RW, Joiner MC, Jones B, Jones DT, van der Kogel AJ, Wambersie A, Whitmore G. Bioeffect modeling and equieffective dose concepts in radiation oncology--terminology, quantities and units. *Radiother Oncol* 2012; **105**: 266-268 [PMID: [23157980](#) DOI: [10.1016/j.radonc.2012.10.006](#)]
- 15 **Garcia-Aguilar J,** Patil S, Gollub MJ, Kim JK, Yuval JB, Thompson HM, Verheij FS, Omer DM, Lee M, Dunne RF, Marcet J, Cataldo P, Polite B, Herzig DO, Liska D, Oommen S, Friel CM, Ternent C, Covelev AL, Hunt S, Gregory A, Varma MG, Bello BL, Carmichael JC, Krauss J, Gleisner A, Paty PB, Weiser MR, Nash GM, Pappou E, Guillem JG, Temple L, Wei IH, Widmar M, Lin S, Segal NH, Cercek A, Yaeger R, Smith JJ, Goodman KA, Wu AJ, Saltz LB. Organ Preservation in Patients With Rectal Adenocarcinoma Treated With Total Neoadjuvant Therapy. *J Clin Oncol* 2022; **40**: 2546-2556 [PMID: [35483010](#) DOI: [10.1200/JCO.22.00032](#)]
- 16 **Solé S,** Baeza R, Gabler C, Couñago F. New standard in locally advanced rectal cancer. *World J Clin Oncol* 2020; **11**: 990-995 [PMID: [33437661](#) DOI: [10.5306/wjco.v11.i12.990](#)]



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>

