

88390\_Auto\_Edited.docx

**Name of Journal:** *World Journal of Clinical Oncology*

**Manuscript NO:** 88390

**Manuscript Type:** EDITORIAL

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

Ke TW *et al.* RT for rectal cancer

Tao-Wei Ke, Yu-Min Liao, Sheng-Chi Chang, <sup>1</sup>Che-Hung Lin, William Tzu-Liang Chen, Ji-An Liang, Chun-Ru Chien

**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 Dec 1;37(34):3223-3233), NCT04165772 (N Engl J Med. 2022 Jun 23;386(25):2363-2376), and PROSPECT (N Engl J Med. 2023 Jul 27;389(4):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

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* 2023; In press

**Core Tip:** 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.

## **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.

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 value 0.12) [11]. However, the disparity in locoregional failure became

more pronounced with borderline statistical significance after extended follow-up (p value 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 (TNT) 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.

ORIGINALITY REPORT

2%

SIMILARITY INDEX

PRIMARY SOURCES

1

[ar.iijournals.org](http://ar.iijournals.org)  
Internet

13 words — 2%

EXCLUDE QUOTES ON  
EXCLUDE BIBLIOGRAPHY ON

EXCLUDE SOURCES < 12 WORDS  
EXCLUDE MATCHES < 12 WORDS