



Letter to the Editor

Comment on ‘Adjuvant chemotherapy in patients with rectal cancer achieving pathologic complete response after neoadjuvant chemoradiation and surgery’

Bin Ma, Qingkai Meng*

Department of Colorectal Surgery, Cancer Hospital of China Medical University, Liaoning Cancer Hospital & Institute, No. 44 Xiaoheyan Road, Dadong District, Shenyang 110042, Liaoning Province, People's Republic of China

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Dear Editor,

We read with great interest the letter published in the *European Journal of Cancer* by Tomasello *et al.* assessing the issue of whether adjuvant chemotherapy is necessary for patients with locally advanced rectal cancer who have achieved pathologic complete response (pCR) [1]. In their letter, Tomasello *et al.* conducted a meta-analysis, and their results indicated that patients with rectal cancer achieving pCR after neoadjuvant chemoradiation should receive 5-fluorouracil-based adjuvant chemotherapy as an improved overall survival (OS) could be observed in the adjuvant chemotherapy group compared with the non-adjuvant chemotherapy group (HR = 0.50, 95% CI = 0.43–0.59, $P < 0.01$). Our team had also published a meta-analysis based on the same issue recently [2]. Although the same conclusion was reached, some issues remain to be discussed.

In their meta-analysis [1], 11 published studies, consisting of 9083 patients, were included, and an overall

analysis was conducted based on OS. However, we do not think that it is appropriate to pool all data from these 11 studies as multiple studies used the same patient population in the same department/database and collection duration. Among the 11 studies, Shahab *et al.* [3], Polanco *et al.* [4], Xu *et al.* [5] and Dossa *et al.* [6] reported outcomes from the same patient population of the National Cancer Database (NCDB), and Gamaleldin *et al.* [7] and Kiran *et al.* [8] both presented outcomes from the same patient population of the Cleveland Clinic Foundation. The overlapped populations may bias the overall analysis and overstate the advantages of adjuvant chemotherapy in patients with rectal cancer with ypCR. In our meta-analysis, we only included the most informative study when multiple studies were published using the same patient population based on the same outcomes. If multiple studies reported different outcomes based on the same patient population, the results were combined for a more comprehensive analysis. Our results indicated that patients with locally advanced rectal cancer with pCR who received adjuvant chemotherapy showed a significantly improved OS when compared with patients with observation only (HR = 0.65, 95% CI = 0.46–0.90, $P = 0.01$) [2].

With the development of precision therapy, the issue of whether all patients with rectal cancer should receive adjuvant chemotherapy has remained controversial

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* Corresponding author: Department of Colorectal Surgery, Cancer Hospital of China Medical University, Liaoning Cancer Hospital, Shenyang 110042, Liaoning Province, China.

E-mail address: mqk1971colorectal@163.com (Q. Meng).

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because limited data have been provided based on different subgroup populations. Routine delivery of adjuvant chemotherapy has been proposed, especially for potential subgroups with a good prognosis. Notably, two recent published analyses based on the NCDB demonstrated that adjuvant chemotherapy associated with improved OS in patients with pCR after neoadjuvant chemoradiotherapy for resected locally advanced rectal cancer [4,6]. Although the meta-analyses conducted by Tomasello *et al.* and our team both indicated that adjuvant chemotherapy should be routinely delivered in patients with rectal cancer with ypCR, the current evidence was mainly based on respective studies. Hence, we need large-scale randomized studies and individual data to update our findings. Meanwhile, other survival outcomes (disease-free survival and local recurrence-free survival) should also be evaluated to comprehensively assess the role of adjuvant chemotherapy in patients with rectal cancer.

Conflict of interest statement

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