



## Local regrowth after ‘Watch and Wait’ strategy: is salvage surgery enough for disease control?

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Dear Editor:

We read with interest On and Aly’s article entitled “Watch and wait in rectal cancer: summary of the current evidence” [1]. The authors offer an overview of the latest achievements in the organ-preserving treatment of locally advanced rectal cancer by neoadjuvant chemoradiotherapy (CRT) in patients with clinical complete response (cCR) reporting an update of common issues related to the Watch and Wait (WW) approach in terms of baseline patients’ selection, CRT regimen, assessment of cCR, and oncologic and functional outcomes.

A conservative treatment, based exclusively on CRT, allows the preservation of the rectum, in patients with a cCR, thus avoiding a more radical surgical treatment and its related morbidity and mortality. This possibility is, however, an ambitious goal as no randomized clinical trials are available so far. As reported in the above-mentioned review, the International Watch and Wait Database (IWWD) [2], the largest series of 880 patients managed by WW, reports a local regrowth (LR) rate of 25% (mostly in the first 2 years of follow up), with a 5-year overall survival (OS) and 5-year disease-specific survival of 85% and 94% respectively.

Even though a meta-analysis reported a better disease free survival (DFS) in patients who had a pathological complete response (pCR) after surgery than in patients managed by WW [3], the feasibility of performing an immediate salvage surgery in the case of LR (88%) has allowed to obtain no

difference in 3-year non-regrowth DFS (that is not including LR) and OS between WW and surgical resection group in a propensity score-matched cohort analysis (the OnCoRe project) [4], quoted by the authors. Furthermore, while LR can be successfully treated by salvage surgery, local pelvic recurrence occurs after surgery which means that the oncological treatment has failed. Indeed, in a systematic review [5], local control of regrowth was confirmed in 83.8% of cases with no difference in OS between patients who had undergone salvage surgery and the WW group. However, in On’s article, few data are provided on distant metastasis (DM), whose incidence increases mainly in those patients that develop an LR.

In the IWWD, DM rate was 8%. Eighteen percent of patients with LR developed DM (38 of 213), whereas only 5% of patients with sustained cCR (not LR) had DM (33 of 634). A 5-year disease-specific survival and OS were 97.3% and 87.9% respectively in sustained cCR group and 84.0% and 75.4% in patients with LR [2]. A recent meta-analysis including 602 patients managed by WW after cCR to CRT reports 10% of DM. Twenty-nine of 436 patients without LR developed DM (7%) while the percentage of patients presenting distant recurrence was, also in this case, more than double in patients with LR (19%) involving 31 of 166 patients [6]. A retrospective analysis of the Memorial Sloan Kettering group compared the oncologic outcomes of 113 patients with cCR after CRT managed with WW strategy and 136 patients who underwent radical surgery with pCR. In spite of obtaining a consistent rate of rectal preservation (82%), there was a significant difference in terms of DM between the patients who had LR (36%) and those without LR (1%) in the WW group ( $p < .001$ ) [7].

DMs were identified mainly after the LR and the most common site was the lung.

These results might lead to believe that, although it is possible to manage LR effectively, it could represent a risk factor for the distant progression of the disease. In addition, the outcomes of the well-known group from São Paulo has highlighted a statistically significant difference in the OS between

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patients without LR after cCR and patients with LR after cCR followed by salvage resection (93.7% vs 63.3%;  $p = 0.03$ ) [8].

Although there is still lack of consistency in the follow-up programs, which are more intensive during the first 2 years to detect recurrence early, for patients with cCR and managed with WW strategy, the presence of a larger number of DMs among patients with LR could suggest the need for longer surveillance protocol in patients with LR and, when it occurs, accurate preoperative systemic restaging to evaluate the use of additional chemotherapy. More information might be provided by randomized phase II trial still in progress (NCT02052921), which will compare the oncologic outcomes between surgical and observational treatment in patients who underwent neoadjuvant CRT for locally advanced rectal cancer with cCR.

## References

1. On J, Aly EH (2018) ‘Watch and wait’ in rectal cancer : summary of the current evidence. *Int J Color Dis* 33(9):1159–1168
2. Van Der Valk MJM, Hilling DE, Bastiaannet E et al (2018) Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database ( IWWD ): an international multicentre registry study. *Lancet* 391:2537–2545
3. Dossa F, Chesney TR, Acuna SA, Baxter NN (2017) A watch-and-wait approach for locally advanced rectal cancer after a clinical complete response following neoadjuvant chemoradiation : a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2(7):501–513
4. Renehan AG, Malcomson L, Emsley R, Gollins S, Maw A, Myint AS, Rooney PS, Susnerwala S, Blower A, Saunders MP, Wilson MS, Scott N, O’Dwyer ST (2016) Watch-and-wait approach versus surgical resection after chemoradiotherapy for patients with rectal cancer ( the OnCoRe project ): a propensity-score matched cohort analysis. *Lancet Oncol* 17(2):174–183
5. Kong JC, Guerra GR, Warriar SK, Ramsay RG, Heriot AG (2017) Outcome and salvage surgery following ‘watch and wait’ for rectal Cancer after neoadjuvant therapy: a systematic review. *Dis Colon Rectum* 60(3):335–345
6. Chadi SA, Malcomson L, Ensor J et al (2018) Articles factors affecting local regrowth after watch and wait for patients with a clinical complete response following chemoradiotherapy in rectal cancer ( InterCoRe consortium ): an individual participant data meta-analysis. *Lancet Gastroenterol Hepatol* 1253(18):1–7
7. Smith JJ, Strombom P, Chow OS, Roxburgh CS, Lynn P, Eaton A, Widmar M, Ganesh K, Yaeger R, Cercek A, Weiser MR, Nash GM, Guillem JG, Temple LKF, Chalasani SB, Fuqua JL, Petkovska I, Wu AJ, Reyngold M, Vakiani E, Shia J, Segal NH, Smith JD, Crane C, Gollub MJ, Gonen M, Saltz LB, Garcia-Aguilar J, Paty PB (2019) Assessment of a watch-and-wait strategy for rectal cancer in patients with a complete response after neoadjuvant therapy. *Jama Oncol* 5(4):e185896
8. Habr-Gama A, São Julião GP, Gama-Rodrigues J, Vailati BB, Ortega C, Fernandez LM, Araújo SEA, Perez RO (2017) Baseline T classification predicts early tumor regrowth after nonoperative management in distal rectal cancer after extended neoadjuvant chemoradiation and initial complete clinical response. *Dis Colon Rectum* 60(6): 586–594

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