Does the addition of induction chemotherapy improve outcome in locally advanced rectal carcinoma?

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Dear Editor:

Locally advanced rectal cancer (LARC) is defined as directly tumor invasion into the pericorectal tissues (T3) and other organs or structures (T4), and/or metastasis in regional lymph node (N+). The treatment of LARC is multidisciplinary, and neo-adjuvant chemoradiotherapy (CRT) followed by surgery is the standard of care in this setting of patients, based on the CAO/ARO/AIO-94 German Rectal Cancer Study. This study compared neo-adjuvant versus adjuvant CRT regimen in a cohort of 823 patients with LARC. Neo-adjuvant CRT improved local control (6 versus 13 %, $p=0.02$), as well as sphincter preservation (39 versus 19 %, $p=0.004$) and decreased acute and late toxicity (27 versus 40 % and 14 versus 24 %, respectively) compared with post-operative CRT.

Year after year, local recurrence has represented the prevailing method of treatment failure. The degree of pathological regression, as well as the pathological complete response (pCR), correlates with a favorable prognosis. Nowadays, with the standardization of total mesorectal excision (TME) surgery and the advance in radiotherapeutic techniques, local tumor control rates have improved, whereas the development of distant metastasis remains the main mode of failure [1–4]. Thus, the reduction in local recurrence rates emphasizes the need to investigate the risk of distant metastases, and therefore the attention shifts to new treatment strategies to improve distant tumor control. Consequently, there is a rationale of adding

induction chemotherapy (CHT): most of LARC recurrences are systemic and induction CHT should be used to better control distant metastasis.

Based on the efficacy demonstrated in stage IV colon cancer patients, the addition of induction chemotherapy should confirm beneficial properties. The theoretical advantage of induction CHT may allow improvement of oxygenation and higher intramural concentration of cytotoxic drugs. Benefit probably includes a tumor down staging and an early eradication of micrometastasis, without affect compliance on subsequent CRT and/or surgery.

The current aim is to evaluate the effect of induction CHT before neo-adjuvant CRT in LARC, to determine whether the induction CHT can assure better overall survival and disease free survival, which is typically achieved by concomitant neo-adjuvant treatment in patients with LARC.

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