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ASO AUTHOR REFLECTIONS

ASO Author Reflections: Addition of Induction Chemotherapy Prior to Neoadjuvant Chemo(Re)Irradiation in Patients with Locally Recurrent Rectal Cancer to Improve Long-Term Outcomes

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PAST

In accordance with the treatment of patients with primary locally advanced rectal cancer, patients with locally recurrent rectal cancer (LRRc) who are radiotherapy-naïve are treated with neoadjuvant chemoradiotherapy.¹ Patients who previously received pelvic radiotherapy may be treated with chemo(re)irradiation, which is standard of care in The Netherlands.² Nevertheless, R0 resections are achieved in only 60% of patients and a pathologic complete response (pCR) is achieved in only 8% of patients. Consequently, these patients continue to have a limited prognosis.^{3,4}

PRESENT

In order to improve the prognosis of LRRc patients, induction chemotherapy may be added to the treatment regimen as this may improve local downsizing and thereby improve the R0 resection and pCR rate. This may eventually lead to improved long-term oncological outcomes in patients with LRRc. The current retrospective study evaluated the effect of this treatment regimen in 132 patients with LRRc. An R0 resection was achieved in 63% of patients, and in 17% of patients a pCR was observed. A pCR translated to an excellent 3-year overall survival of 92% in these patients. Moreover, pathologic response

proved to be an independent predictor for local recurrence-free survival, metastasis-free survival, and disease-free survival, whereas R0 resection was an independent predictor for local recurrence-free and overall survival in patients without synchronous metastases. When combining these two independent predictive variables, patients with a Mandard score of 2–3 and an R0 resection showed an outcome almost as good as patients with a pCR. This emphasized the importance of achieving a good response.⁵

FUTURE

This study showed promising results after treatment with induction chemotherapy and chemo(re)irradiation in patients with LRRc. Future research may focus on whether a correlation exists between radiological and pathological response, potentially providing an opportunity to change treatment decisions, e.g. a more extensive preoperative treatment if tumour regression is not sufficient. Ultimately, a randomized controlled trial is warranted to determine whether the addition of induction chemotherapy in the treatment of LRRc improves outcomes for curative treatment of LRRc in general. Therefore, we are currently setting up a multicenter, randomized controlled trial that will randomize 364 patients to receive either neoadjuvant chemoradiotherapy or induction chemotherapy followed by neoadjuvant chemoradiotherapy, prior to surgery. Several European societies have pledged their support. The trial is expected to commence later in 2020.

DISCLOSURES Eva L. K. Voogt, Pim W. A. Burger, and Harm J. T. Rutten declare no conflict of interest.

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