

Reply to: Use of induction chemotherapy in locally advanced rectal cancers to increase the response rates: Is it actually helping?

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Reply to: Use of induction chemotherapy in locally advanced rectal cancers to increase the response rates: Is it actually helping?



Keywords:

Locally advanced rectal cancer
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 Chemoradiotherapy
 Total neoadjuvant therapy
 Pathological complete response
 Clinical complete response

We thank Patel et al. for their comments to our recent manuscript. Although the results of our case-control matched study suggest that the addition of induction chemotherapy to neoadjuvant chemoradiotherapy in patients with prognostically poor LARC results in a higher CR rate than neoadjuvant chemoradiotherapy alone, we recognise that selection bias may have been present. Therefore, we acknowledge in our conclusion that no definitive recommendations can be made and further research is necessary.

The age distribution in our cohort is indeed elderly, which makes this cohort a true representation of the patients in our country: over 50% of patients are aged 70 years or older at the time of diagnosis in the Netherlands. This is also the case when looking to Europe and the United States of America. Although there are global differences, we feel that there is a high applicability of the results.

We agree with Patel et al. that younger patients more often present with poorly differentiated tumours. In a previous study we observed that young patients more frequently presented with signet cell carcinomas compared to older patients (2.6% versus 0.6%) [1]. Nevertheless, the presence of this unfavourable histology was rare, even in younger patients. Given the low prevalence and the small cohort we studied, we did not take the histology into account when performing our statistical analyses.

Despite the fact that matching was performed on tumour stage and MRF involvement, the extent of surgery was different between the two treatment groups with more extended surgeries in the induction chemotherapy group. This does not necessarily mean that the induction chemotherapy was not sufficient in downsizing the tumour in these patients. Generally, the resection planes are determined based on the initial tumour, i.e. the tumour before neoadjuvant treatment. Even when restating MRI shows partial fibrosis, our surgeons prefer to base their margins on the initial imaging since

cutting through fibrosis holds the risk of cutting through tumour, leading to a much worse situation. Although matching on T stage and MRF was performed, possibly the tumour growth beyond the mesorectal fascia was more extensive in the group treated with induction chemotherapy, causing the more extended surgeries.

Patel et al. state that in the chemoradiotherapy group a poorer disease biology is present. We feel it is not possible to make this statement as in the induction chemotherapy group an abdominoperineal resection and extended resection accounted for 60% of the interventions, whereas in the chemoradiotherapy group this accounted for 54%. Therefore, you may not conclude that stage of disease was different.

We agree that lateral lymph nodes are a poor prognostic factor. In the MEND-IT trial, a single-arm, prospective trial including patients with prognostically poor LARC that is currently being set up in the Netherlands, this is therefore one of the inclusion criteria. Furthermore, the presence of MRF involvement, grade 4 mrEMVI and tumour deposits are criteria for inclusion. We await this and other studies before drawing any definitive conclusions regarding the use of induction chemotherapy in high-risk locally advanced rectal cancer.

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Disclosure

None.

Declaration of competing interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Reference

- [1] Orsini RG, Verhoeven RHA, Lemmens VEPP, Van Steenberghe LN, De Hingh IHJT, Nieuwenhuijzen GAP, et al. Comparable survival for young rectal cancer patients, despite unfavourable morphology and more advanced-stage disease. *Eur J Canc* 2015;51(13):1675–82. <https://doi.org/10.1016/j.ejca.2015.06.005>.

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E.L.K. Voogt*, D.P. Schaap
Department of Surgery, Catharina Hospital, Eindhoven, the
Netherlands

K. van den Berg
Department of Medical Oncology, Catharina Hospital, Eindhoven, the
Netherlands

G.A.P. Nieuwenhuijzen, J.G. Bloemen
Department of Surgery, Catharina Hospital, Eindhoven, the
Netherlands

G.J. Creemers, J. Willems
Department of Medical Oncology, Catharina Hospital, Eindhoven, the
Netherlands

J.S. Cnossen, H.M.U. Peulen
Department of Radiation Oncology, Catharina Hospital, Eindhoven,
the Netherlands

J. Nederend
Department of Radiology, Catharina Hospital, Eindhoven, the
Netherlands

G. van Lijnschoten
Pathology Department, PAMM Laboratory for Pathology and Medical
Microbiology, Eindhoven, the Netherlands

J.W.A. Burger
Department of Surgery, Catharina Hospital, Eindhoven, the
Netherlands

H.J.T. Rutten
Department of Surgery, Catharina Hospital, Eindhoven, the
Netherlands

GROW School for Oncology and Developmental Biology, Maastricht
University, Maastricht, the Netherlands

* Corresponding author. Department of Surgery, Catharina Hospital
Eindhoven, Michelangelolaan 2, 5623 EJ, Eindhoven, the
Netherlands.
E-mail address: eva.voogt@catharinaziekenhuis.nl (E.L.K. Voogt).

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