The need for post-mastectomy radiotherapy in patients with IBC

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We have read with great interest the Review by Tryfonidis *et al.* (Management of locally advanced breast cancer—perspectives and future directions. *Nat. Rev. Clin. Oncol.* 12, 147–162, 2015), which discussed the management of locally advanced breast cancer (LABC). In this article, the authors analysed the main evidence that guides the current therapeutic approach in this heterogeneous disease, which also includes inflammatory breast cancer (IBC).

To illustrate the current therapeutic approach for patients with LABC and IBC, the authors propose an algorithm based on the Advanced Breast Cancer International Consensus Guidelines.2 In patients with IBC who respond to preoperative systemic therapy, these guidelines recommend mastectomy without breast reconstruction plus axillary lymph-node dissection, followed by adjuvant endocrine and/or anti-HER2 therapy per indication based on the molecular profile of the tumour.^{1,2} However, an issue we would like to highlight is the absence of recommendation of radiotherapy after mastectomy for patients in this group. IBC is a rare and aggressive form of breast cancer,3 and patients with this cancer have a probability of lymph-node involvement ranging from 55% to 85%.3,4

Since the 1970s, the treatment of women with IBC has been based on the combination of chemotherapy, surgery, and radiotherapy. This multimodal approach was reached by consensus, and is based on observational studies and/or data extrapolated from patients with locally advanced non-inflammatory tumours. Although a survival benefit for postmastectomy radiotherapy has not been proven in clinical trials, evidence indicates that radiation treatment improves locoregional control, supporting the use of this modality in treatment protocols.⁵

Specifically, a retrospective, singleinstitution, observational study compared

data from 192 patients who completed the planned course of chemotherapy, mastectomy, and postmastectomy radiotherapy with data from 64 patients who did not complete triple therapy, mainly because of a poor response. Of these, 21 patients received preoperative radiotherapy because of lack of response to systemic treatment. A further 21 patients had extended disease and therefore opted to receive radiotherapy alone, and 22 patients suffered post-mastectomy local recurrence before radiotherapy. All the patients who had responded to chemotherapy then underwent mastectomy and received radiotherapy. The investigators observed that the 192 patients that completed the triple modality treatment had significantly better 5-year locoregional control, distant metastasis-free survival and overall survival rates than those who could not complete the treatment as planned. Moreover, a multivariate analysis showed that inability to complete chemotherapy, surgery and radiotherapy treatment was independently associated with worse outcomes based on these end points.6

Similarly, Rueth *et al.*⁷ retrospectively analysed data from 10,197 patients who underwent surgical treatment for nonmetastatic IBC between 1998 and 2010. The 5-year and 10-year survival rates in patients receiving chemotherapy, surgery and post-surgery radiotherapy were higher than for patients who were treated with chemotherapy and surgery alone (55.4% and 37.3% versus 42.9% and 28.5%, respectively).

The second Advanced Breast Cancer International Consensus Guidelines recommend locoregional radiotherapy, even when a pathological complete response is achieved with systemic therapy.² Furthermore, breast cancer treatment guidelines published by the National Comprehensive Cancer Network recommend neoadjuvant chemotherapy followed by mastectomy and postmastectomy

radiotherapy, without distinguishing between the type of response to the systemic treatment.8 In conclusion, despite the lack of data from clinical trials specifically testing radiotherapy in this setting, we believe that it is necessary to include postmastectomy radiotherapy in the treatment algorithm for patients with IBC who respond to neoadjuvant chemotherapy, given the recommendations of international boards of experts and the evidence mentioned in this correspondence.

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Competing interests

The authors declare no competing interests.

- Tryfonidis, K., Senkus, E., Cardoso, M. J. & Cardoso, F. Management of locally advanced breast cancer—perspectives and future directions. *Nat. Rev. Clin. Oncol.* 12, 147–162 (2015).
- Cardoso, F. et al. ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2). Ann. Oncol. 25, 1871–1888 (2014).
- Anderson, W. F., Schairer, C., Chen, B. E., Hance, K. W. & Levine, P. H. Epidemiology of inflammatory breast cancer (IBC). *Breast Dis.* 22, 9–23 (2005).
- Yamauchi, H. et al. Inflammatory breast cancer: what we know and what we need to learn. Oncologist 17, 891–899 (2012).
- Woodward, W. A. & Cristofanilli, M. Inflammatory breast cancer. Semin. Radiat. Oncol. 19, 256–265 (2009).
- Bristol, I. J. et al. Locoregional treatment outcomes after multimodality management of inflammatory breast cancer. Int. J. Radiat. Oncol. Biol. Phys. 72, 474–484 (2008).
- Rueth, N. M. et al. Underuse of trimodality treatment affects survival for patients with inflammatory breast cancer: an analysis of treatment and survival trends from the National Cancer Database. J. Clin. Oncol. 32, 2018–2024 (2014).
- Gradishar, W. J. et al. Breast cancer version 3.2014. J. Natl Compr. Canc. Netw. 12, 542–590 (2014).