



EDITORIAL

Triple negative cT1N0 breast cancer: A matter of millimeters



Cáncer de mama triple negativo cT1N0: cuestión de milímetros

Triple-negative breast cancer (TNBC) has been and still is an inexhaustible source of clinical research, meetings, controversies, and scientific literature. And the reason is clear: for those of us who treat breast cancer, TNBC remains one of our great causes for concern, if not of bitter frustration in the face of therapeutic failure. For this reason, this article by García Torralba et al. is pertinent, because it addresses in a thorough and careful review one of the controversial issues (one more) of the TNBC: whether neoadjuvant is indicated in tumors with stage cT1cN0.

And it could be controversial because initially the neoadjuvant strategy was conceived as a useful tool to reduce the size of the primitive tumor and facilitate conservative surgery, always preferable to mutilating mastectomy. So, neoadjuvant in a cT1 tumor, that is less than 2 cm, runs the risk of becoming overtreatment, because in reality, this is the controversy that underlies the question of the article by García Torralba et al.: are we overtreating cT1c TNBCs?

However, in this scenario, there was a paper that changed everything: Cortázar's 2014¹ review, which showed that obtaining pathological complete remission, pCR, after neoadjuvant became a powerful prognostic factor not only for the prolongation of disease-free survival (DFS) but also for overall survival (OS). This work modified our view of neoadjuvant therapy, making us understand that there are other elements that justify its use and represent an advantage for patients beyond the reduction of tumor size: essentially that we get evidence on the sensitivity of the tumor to treatment by obtaining (or not) the pCR. But in the case of TNBC, it also allows us to provide a second chance to patients who do not obtain pCR, with adjuvant treatment with capecitabine according to the CREATE X study,² or with olaparib in patients carrying BRCA1–2 mutations.³

In recent years, another new quality element has been introduced in the neoadjuvant of TNBC: the immunotherapy with pembrolizumab. However, in the pivotal studies with this drug, especially KEYNOTE 522,⁴ T1 tumors were

expressly excluded, so for the time being their use in the neoadjuvant of cT1 tumors is not indicated, as reflected in the ESMO⁵ and ASCO⁶ guidelines. In reference to the guidelines, they all agree that neoadjuvant treatments of cT1a and cT1b tumors would probably be an overtreatment that is not indicated. Which introduces another element: since we are talking about millimeter difference (< 10 mm for T1b and > 10 mm to consider them as T1c), the accuracy of the radiological assessment becomes even more important.

All this leads us to a conclusion, in addition to those already provided by García Torralba's work: that early TNBC is an exercise in virtuous multidisciplinary collaboration between the different specialists who are involved in its diagnosis and treatment, because—this time yes—the difference between correct treatment and overtreatment can be a matter of millimeters. Very few millimeters.

References

1. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. *Lancet Lond Engl*. 2014 Jul 12;384(9938):164–72.
2. Masuda N, Lee SJ, Ohtani S, Im YH, Lee ES, Yokota I, et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. *N Engl J Med*. 2017 Jun 1;376(22):2147–59.
3. Tutt ANJ, Garber JE, Kaufman B, Viale G, Fumagalli D, Rastogi P, et al. Adjuvant olaparib for patients with BRCA1- or BRCA2-mutated breast cancer. *N Engl J Med*. 2021 Jun 24;384(25):2394–405.
4. Schmid P, Cortes J, Dent R, Pusztai L, McArthur H, Kümmel S, et al. Event-free survival with pembrolizumab in early triple negative breast cancer. *N Engl J Med*. 2022 Feb 10;386(6):556–67.
5. Loibl S, André F, Bachelot T, Barrios CH, Bergh J, Burstein HJ, et al. Early breast cancer: ESMO clinical practice guideline for

- diagnosis, treatment and follow-up. *Ann Oncol Off J Eur Soc Med Oncol*. 2024 Feb;35(2):159–82.
6. Korde LA, Somerfield MR, Carey LA, Crews JR, Denduluri N, Hwang ES, et al. Neoadjuvant chemotherapy, endocrine therapy, and targeted therapy for breast cancer: ASCO guideline. *J Clin Oncol Off J Am Soc Clin Oncol*. 2021 May 1;39(13):1485–505.

J. Ignacio Chacon
*Servicio de Oncología Médica, Hospital Universitario de
Toledo, Toledo, Spain*
E-mail address: jignaciochacon@gmail.com