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Neoadjuvant systemic treatment for breast cancer in Italy: The Italian Society of Surgical Oncology (SICO) Breast Oncoteam survey

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ABSTRACT

The Italian Society of Surgical Oncology (SICO) Breast Oncoteam developed a survey to explore the state of the art of neoadjuvant treatment for breast cancer in Italy, specifically focusing on cases treated during the two-year period 2014–2015.

A questionnaire was sent to Italian Breast Units with a minimum of 150 new breast cancer cases treated/year according to the Senonetwork directory and to the SICO Breast Oncoteam Breast Unit network.

A total of 23/107 Breast Units submitted the survey, reporting a total amount of 20156 cases of breast carcinoma (17241 invasive, 2915 in situ) treated in the biennium, corresponding approximately to 20% of newly diagnosed breast cancers in Italy.

In the United States, medical treatment before surgery for breast cancer is indicated in about 22.7% of newly diagnosed cases according to the National Cancer Database, while a German study reported approximately 20% of cases treated with neoadjuvant therapy. In our survey, a total of 1673/17241 cases (9.7%) were treated with neoadjuvant therapy, ranging from 2.9% to 23.6% according to different centres,

Abbreviations: NAT, NeoAdjuvant systemic Treatment; SICO, Italian Society of Surgical Oncology; DTMP, Diagnostic Therapeutic and Healthcare Management Protocol; QoL, Quality of Life; Fig, Figure.

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showing heterogeneity in neoadjuvant treatment indications, even in multidisciplinary breast units. Better resources should be engaged to achieve a standardised quality indicator for neoadjuvant treatment, and this indicator could be included among the European Society of Breast Cancer Specialists (EUSOMA) quality indicators. In the near future, we plan to develop a second survey to better test improvements in the employment of neoadjuvant therapy after the expiry of the 2016 European Parliament deadline and after the 2017 St. Gallen Conference recommendations.

Introduction

Initially developed as a treatment option for locally advanced breast tumours, the concept of neoadjuvant systemic treatment (NAT) has, over the years, been translated into the setting of early breast cancer [1,2].

NAT can be employed to downstage a tumour and therefore to achieve loco-regional disease control allowing breast surgery in initially unresectable neoplasms [3].

The rationale of primary systemic treatment for operable breast cancers is the opportunity to test in vivo chemosensitivity, instead of administering adjuvant treatment after tumour removal [4]. In fact, recent meta-analyses have shown how pathologic complete response (pCR) after NAT can occur in around 20% of cases and how it is associated with a better prognosis [5,6].

Primary systemic treatment can convert a surgical indication for mastectomy into a conservative option (breast conservative surgery, nipple/skin sparing mastectomies with immediate reconstruction) [7,8] and can downstage axillary node-positive disease to node-negative [9,10].

In order to select those patients most likely to respond to NAT and thus avoid unnecessary aggressive treatments, molecular biomarkers are required.

The wide range of responses to NAT is related to histotype (ductal/lobular/other types), to molecular subtypes of breast cancer (Luminal A, Luminal B, HER2-enriched, and triple negative) and to the proliferation index. Triple negative and even more HER2-enriched subtypes, particularly in the absence of hormone receptor expression, show a higher rate of pCR, while luminal B/HER2-negative subtypes demonstrates a lower rate of pCR [5,11]. Only a minority of patients affected by Luminal A subtypes and lobular histotype achieve pCR [11,12].

Pre-surgical systemic treatment can include chemotherapy regimens (in the majority of cases), associated with anti-HER2 targeted agents in HER2-overexpressed tumours, or endocrine therapy that could represent an option in clinical trials for hormonal sensitive cancers [13].

The aim of the present survey is to estimate the current employment of NAT for breast cancer treatment in Italy and the current modalities.

Materials and methods

In July 2016, the Italian Society of Surgical Oncology (SICO) Breast Oncoteam developed a questionnaire involving various aspects of NAT and specifically referred to cases treated during the two-year period 2014–2015. The questionnaire was divided into 7 sections: general information, clinical records, indications, diagnosis, surgical treatment, radiation therapy, and final considerations (Table 1). It was sent by e-mail to all the Italian Breast Units which handle a minimum of 150 new breast cancer cases treated per year, according to the Senonetwork directory [14] and to the SICO Breast Oncoteam Breast Unit network. The authors certify that ethical approval was not required for the study.

Descriptive analysis was carried out as appropriate.

Results

A total of 23/107 (21,4%) Breast Units completed and submitted the survey to the SICO Breast Oncoteam, reporting a total of 20156 cases of breast carcinoma (17241 invasive carcinoma, 2915 in situ) treated in the 2014–2015 biennium. A total of 1673 of 17241 cases (9.7%) were treated with NAT, ranging from 2.9% to 23.6% according to different centres.

Unfortunately, it was not possible to report T and N status before NAT, due to the lack of information from many centres. Breast pathological response was complete (ypT0 and ypTis in the definitive histological examination) in 538 from 1673 cases (32,1%), 410/1673 (24,5%) ypT0 and 128/1673 (7,6%) ypTis respectively (Fig. 1).

In 859 cases, pathological nodal status after NAT was negative, ypN0 and ypN0sn, with a total of 21 (91.3%) centres performing sentinel node biopsy in clinically node-negative patients pre-NAC and 14 (60.8%) centres performing sentinel node biopsy in patients with nodal involvement pre-NAC who showed a complete radiological response. A total of 17 (73.9%) centres reported a sentinel node detection rate >90% post NAT, 2 centres <90%. In 15 (65.2%) centres, the tracer employed is ^{99}Tc only, 4 centres employ the double tracer technique with ^{99}Tc and blue dye, one centre uses indocyanine green, while 3 (13%) centres did not respond to the question.

In all centres, a Diagnostic, Therapeutic and Healthcare Management Protocol (DTMP) is active and the final planning decision is discussed during multidisciplinary meetings. The major indication reported for NAT is biological subtype (86.4%), as shown in Fig. 2 and, in relation to the biological subtypes, all the 23 Breast Units indicate NAT for HER2+ tumours, 21 (91.3%) for triple-negative tumours, 15 (65.2%) for luminal B cancers, while only 5 (21.7%) multidisciplinary groups indicate NAT for luminal A cancers (Fig. 3). In 14 centres, HER2 status is considered crucial for preoperative treatment indication in all cases, while in the remaining 9 centres it is considered only for selected cases. Among the 1673 reported cases treated with NAT, 527 (31.5%) were HER2 positive cases. In 17 breast units, neoadjuvant endocrine therapy is employed.

Regarding diagnostic procedures, although there may be some concerns regarding the actual need for staging in asymptomatic patients according to the recent guidelines [15], we enquired about the procedures employed. We found that 54.5% of centres perform a CT total body and a skeletal scintigraphy; the other centres reported that they conduct positron emission tomography only (17.4%), positron emission tomography and skeletal scintigraphy (13%), positron emission tomography or CT total body (8.7%), or CT total body only (4.3%).

Also regarding breast diagnostic procedures, in 17 breast units, pre- and post-NAT Breast MRI is performed for every

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