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Can multigene assays widen their clinical usefulness in early breast cancer treatment choice during the current COVID-19 outbreak in Italy?

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The European severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has had its first epicentre in Italy. Although a relative slowdown of the contagion spread has been anticipated, we are very far from resuming our regular activities, including those related to the healthcare organisation. Rather, we will have to rearrange our healthcare system to mitigate the risk of SARS-CoV-2 particularly in the frail population, including breast cancer (BC).

As a matter of fact, one of the issues for the breast units in the near future might be the convenience to defer surgery and to spare chemotherapy (CT), whenever endocrine therapy (ET) could be considered an optimal treatment. Multigene assays (MGAs), including the Oncotype DX, MammaPrint/BluePrint, EndoPredict and Prosigna/PAM50, have been endorsed for few years by different scientific cancer societies, including ESMO,[1] as part of the decision process in selecting adjuvant treatment for luminal early BC. Actually, the clinical utility of MGAs is fully established in the adjuvant setting while it is suggested in the neoadjuvant setting.

In the emergency phase of the COVID-19 outbreak, the role of neoadjuvant endocrine therapy (NET) is somehow perceived of relevant importance. Herein, the clinical studies evaluating the role of MGAs in HR+/HER2– early BC treated with NET are briefly described (table 1). Two of these MGAs, Oncotype DX and EndoPredict, have shown a correlation between test results and response to NET suggesting a clinical utility to guide NET treatment decisions.

The Oncotype DX has been validated in the neoadjuvant setting to predict clinical response to NET in HR+/HER2– early BC. The TransNEOS study of recurrence score (RS) demonstrated that a significant higher proportion of patients with RS <18 had a clinical response with preoperative Letrozole (55%) versus patients with RS ≥31 (22%) (p<0.001).[2] Moreover, results of ABCSG34 study with EndoPredict (EP) have shown that HR+/HER2– early BC patients with a low risk EP score had a higher probability to respond to NET (27%) as compared with only 8% for high risk EP score (p=0.024).[3] Results observed in a cohort of HR+/HER2– early BC, in the context of the NBRS Trial, showed that 68% of patients with BluePrint Luminal tumours receiving NET reached a clinical response.[4] Finally, in the CORALLEEN

Table 1 Principal clinical trials evaluating the role of MGAs in patients receiving NET in early BC

	Patient no.	Subtype	Treatment	Endpoint	Results	Clinical validation*	Trial (ref)
Oncotype DX	295	HR+/HER2–	NET	Clinical response	55% (RS <18) versus 22% (RS >31)	Yes	TransNEOS[2]
Endopredict	83	HR+/HER2–	NET	RCB 0/1	27% (EP low) versus 7% (EP high)	Yes	ABCSG34[3]
Mammaprint/ BluePrint	53	HR+/HER2–	NET	Clinical response	68% BluePrint Luminal	No	NBRST[4]
Prosigna (ROR)	106	High-risk Luminal BC	NET/TT versus NAC	Low ROR at surgery	46.9% NET/TT versus 46.1% NAC	No	CORALLEEN[5]

*Clinical validation: MGAs demonstrating a statistical correlation to predict patients' outcome.
NAC, Neadjuvant chemotherapy; NET, neoadjuvant endocrine therapy; RCB, residual cancer burden; ROR, risk of recurrence; TT, Letrozole+Ribociclib.

study, the activity of neoadjuvant Letrozole+Ribociclib (NET/TT) obtained similar ROR molecular downstaging as compared with standard NAC (46.9% vs 46.1%, respectively).[5]

Therefore, it seems that MGAs can now provide clinical utility to select early BC luminal patients who might be considered for NET with the aim of reducing risks of infection during pandemic. Currently, in Italy, only 2 out of 20 regions provide reimbursement for MGAs in selected HR+/HER2− early BC patients. This condition causes an evident missed opportunity which, although hardly justifiable in ordinary healthcare conditions, becomes even more unacceptable in this pandemic, when optimisation of care should be a top priority. We wonder whether this should be the right time for Italy to promptly provide national reimbursement for MGAs in selected patients to support optimal BC treatment choices during pandemic.

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REFERENCES

1 Cardoso F, Kyriakides S, Ohno S, *et al*. ESMO guidelines Committee. *Ann Oncol* 2019;30:1674.
2 Iwata H, Masuda N, Yamamoto Y, *et al*. Validation of the 21-gene test as a predictor of clinical response to neoadjuvant hormonal therapy for ER+, HER2-negative breast cancer: the TransNEOS study. *Breast Cancer Res Treat* 2019;173:123–33.
3 Dubsky PC, Fesl C, Singer CF, *et al*. *The EndoPredict score predicts residual cancer burden to neoadjuvant chemotherapy and to Neo-Endocrine therapy in HR+/HER2- breast cancer patients from ABCSG 34. SABCS Dec 5-9*, 2017.
4 Whitworth P, Beitsch P, Mislowsky A, *et al*. Chemosensitivity and endocrine sensitivity in clinical luminal breast cancer patients in the prospective neoadjuvant breast registry symphony trial (NBRST) predicted by molecular subtyping. *Ann Surg Oncol* 2017;24:669–75.
5 Prat A, Saura C, Pascual T, *et al*. Ribociclib plus letrozole versus chemotherapy for postmenopausal women with hormone receptor-positive, HER2-negative, luminal B breast cancer (CORALLEEN): an open-label, multicentre, randomised, phase 2 trial. *Lancet Oncol* 2020;21:33–43.