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JNCI J Natl Cancer Inst (2016) 108(8): djw105

doi: 10.1093/jnci/djw105
First published online July 4, 2016
Response

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We thank Toomey and colleagues from the Royal College of Surgeons of Ireland for submitting their observations related to use of the RNA Disruption Assay (RDA) in the early prediction of pathological complete response (pCR) outcomes in the TCHL (docetaxel, carboplatin, trastuzumab +/- lapatinib) phase II clinical trial (1). Their work supports RDA as a biomarker for pCR in human epidermal growth factor receptor 2 (HER2)–positive breast cancer.

They independently show that high RDA scores obtained from core biopsies taken 20 days after the first dose of chemotherapy plus targeted therapy correlate with significantly higher chance of pCR. As well, tumor content from these biopsies was significantly less for the patients who later achieved pCR.

In our previous work, we have shown that tumor cellularity at mid-treatment biopsy did not correlate with eventual pCR (2); however, these differences may be due, as Toomey et al. point out, to the rapid response to anti-HER2 therapy in HER2-positive disease compared with other receptor subtypes.

In the MA22 National Cancer Institute of Canada Clinical Trials Group phase II trial of combined epirubicin and docetaxel in locally advanced breast cancer (3,4), patients with high tumor RDA scores achieved better long-term disease-free survival regardless of receptor status or whether pCR was achieved.

Using RDA, tumors can be divided into three categories—those with high, mid, or low tumor RNA disruption. We hypothesize that those tumors with low disruption are unlikely to respond to the treatment being given. These patients may benefit from an early change in treatment strategy, an idea that warrants further investigation.

In unpublished data, RDA scores can be measured in breast cancer early in the first cycle of chemotherapy by fine needle aspiration (FNA), again with correlation of high RDA and pCR. This observation was obtained in a single center, and we are currently carrying out a multicenter trial to confirm the correlation. Although core biopsy material can be used, FNA carried out in the clinic setting may enable widespread use of this simple, inexpensive modality to easily obtain tissue with little morbidity for the patient.

In the search for response-guided therapy in primary systemic therapy, RDA warrants further investigation as a potential candidate with both prognostic and predictive benefits. Women with breast cancer will benefit from the knowledge that their treatment is effective and if not will benefit perhaps from a switch in therapy and avoidance of further side effects from ineffective treatment.

References

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Received: March 8, 2016; **Accepted:** March 9, 2016