[P3-06-35] Association of estrogen receptor (ER) levels and prediction of antiproliferative effect of hormone therapy (HT) in lower ER-expressing tumors

Dixon JM, Turnbull A, Renshaw L, Rothney MP, Loman CA, Arthur L, Thomas JS, Young O, Murray J, Williams L, Sing AP, Cameron D. Edinburgh Breast Unit, Edinburgh, Midlothian, United Kingdom; Edinburgh University, Edinburgh, Midlothian, United Kingdom; Genomic Health Inc, Redwood City, CA

Intro

Accurate measurement of ER in early stage invasive breast cancer (EBC) is important to identify patients likely to benefit from HT. While immunohistochemistry (IHC) is the most common method to quantify ER, other methods can also accurately measure ER, such as RT-PCR. ER is one of the genes included in the RT-PCR based 21-gene Recurrence Score assay (Onco*type* DX®, Genomic Health, Redwood City, CA) and is also reported separately as a single gene expression. Additionally, the association between ER expression by RT-PCR (ER-PCR) and tamoxifen benefit has been reported by Kim, et al (2011). A recent study reported that patients with ER levels <10% by IHC were largely negative by RT-PCR (Singh, et al; 2014) and that this has potential implications for which patients may be expected to benefit from HT. Robust measures of ER and the proliferative response may be useful in identifying patients likely to respond to HT.

Aim

The study aims are: (1) To correlate quantification of ER in EBC as assessed by Allred Score (AS) and ER as measured by RT-PCR in the 21-gene assay; (2) To describe changes in ER, Recurrence Score, and measures of proliferation after 2wks of an aromatase inhibitor (AI); (3) To perform exploratory analyses of factors associated with changes in proliferation.

Methods

55 postmenopausal EBC patients with lower ER (AS 2-7) were treated with 2wks of an AI followed by wide excision. All patients had a 21-gene assay on a pre-and post-treatment (Tx) sample. Proliferation was measured by both Ki67 by IHC (in 45 patients) and by the proliferation gene group score (PGS) in the RT-PCR based 21-gene assay (in all patients). Proliferation response was defined by a 20% relative decrease in Ki67 or a decrease in PGS. Changes in proliferation were correlated with AS, ER-PCR and Recurrence Score result.

Results

The Table shows the correlation of AS with ER-PCR measured in the pre-Tx (r=0.83) samples. 94% of AS (2-3) patients and 56% of AS (4-5) were ER(-) by RT-PCR There was a significant change (pre to post) in the average Ki67 level (18% to 11%; p<0.001) and PGS but not Recurrence Score result. 37/45 patients showed a 20% decrease in Ki67 while only 32/55 had a decrease in PGS. Changes in Ki67 levels were greatest in AS 6/7 patients with a 76% relative decrease vs 21% in AS 2/3 patients. The range of PGS change was 1% increase in AS 2/3, 1% decrease in AS 4/5 and 14% decrease in AS 6/7 patients. Univariate predictors of decrease in Ki67 were AS of 5/6/7 (vs 2/3/4), Recurrence Score result, ER-PCR (continuous or binary), and PR-PCR. The same variables were predictors of PGS change.[table1]

Conclusions

- Results confirm earlier reports showing substantial disagreement in ER measured by IHC vs RT-PCR in patients with lower ER-expressing tumors
- The clinical implications are that a substantial number of patients with low ER by IHC may have little to no benefit from HT
- The 21-gene assay may be useful in selecting patients likely to benefit from HT
- Further studies in larger cohorts are required to confirm these findings.