INTEGRATIVE ANALYSIS OF TWO PROSPECTIVE NEOADJUVANT STUDIES WITH BREAST CANCER PATIENTS AND MICROARRAY ANALYSIS

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Aim: Two prospective studies were designed to examine the feasibility of gene expression profiling to predict pathological response in early breast cancers. We present long-term outcome data as well as association of gene expression with clinical data.

Methods: Clinical characteristics of two consecutive prospective phase II neoadjuvant studies were examined. Eligible criteria included stage IIA-IIIC, chemotherapy-naive, measurable disease, age >20, PS 0/1, adequate organ function. Neoadjuvant treatment included anthracyclin-based regimens plus taxane with or without trastuzumab. cDNA microarray by Affimetrix Gene Chip U133 plus 2.0 arrays with 54613 genetic variables from pretreatment fine-needle biopsy specimens was performed.

Results: Between December 2005 and December 2013, 107 patients were enrolled and followed up. Median follow up time was 50.8 months (13.2-92.7). Median age 51 (23-76), PS 0:1=100:7, stages IIA:IIB:IIIA:IIIB:IIIC=23:50:19:14:1, HER2-/ER+:HER2+/ER+:HER2+/ER-:HER2-/ER-=48:13:23:23. Pathological complete response (pCR) rate was 28%. pCR rate was significantly higher in HER2+ plus ER+, HER2+ plus ER-, and HER2+ plus ER- breast cancers compared to HER2- plus ER+ cancers (p=0.0006, p=0.013, p=0.0218 respectively), and lymph node (LN) negative cancers compared to LN 1-3 positive cancers (p=0.0098). Five year disease free survival (DFS) was 77.7% (HER2-/ER+:HER2+/ER+:HER2+/ER-:HER2-/ER-= 75.8%:92.3%:86.7%:60.9%). Significant prolonged DFS was seen in HER2-/ER+ cancers compared to HER2-/ER- (p=0.0008), and LN negative cancers compared to LN>=4 (p=0.0025). No significance was seen between DFS and pCR. Total cDNA microarray data of 78 of 107 patients was available. For DFS, 17 most-associated genes were identified. The associated genes were evaluated using Cox regression, and low-risk classification identified patients (n=46) showed improved DFS than the high-risk group (n=33) (HR 70.0, p=0.004). For pCR, 8 specific genes were identified as having a relation.

Conclusions: Clinical characteristics from long term follow up of two prospective studies were shown. Microarray analysis enabled us to identify preliminary data of specific genes associated with breast cancer recurrence and pCR respectively. Further clinical follow-up and validation tests are to follow.

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