MESENCHYMAL CIRCULATING TUMOUR CELL ANALYSIS TO PREDICT EFFICACY OF ERIBULIN FOR METASTATIC BREAST CANCER PATIENTS

Yoshiya Horimoto, Emi Tokuda, Fumi Murakami, Katsuya Nakai, Hideo Shimizu, Mitsue Saito
Juntendo University School of Medicine, Dept. of Breast Oncology, Tokyo, Japan

Background: While there are as yet no established tools or markers for predicting breast cancer treatment effects, liquid biopsy approaches, such as measuring circulating tumour cells (CTCs) and cell-free DNA, have recently been introduced in both preclinical and clinical studies. CTC analyses are well developed and the epithelial mesenchymal transition (EMT) status of CTCs can now also be assessed. We investigated CTCs in metastatic breast cancer patients who had received Eribulin, which reportedly suppresses EMT as a mechanism of tumour suppression, to test the possibility of this method serving as a tool for predicting Eribulin efficacy.

Methods: Nine patients have thus far been enrolled and peripheral blood samples (10 ml) were collected before Eribulin treatment and examined. Seven patients developed metastatic disease after curable surgery for primary breast cancer, while two had Stage IV disease. CTCs were examined using a Microfluidic Chip device at Nihon Gene Research Laboratories (Japan). CTCs positive for pan-cytokeratin and vimentin were defined as epithelial and mesenchymal CTCs, respectively.

Results: Mean patient age at the time of starting Eribulin was 62 years. Median disease free survival after curable surgery was 71 months (range 16-125). The intrinsic subtype rates of the primary tumours were: luminal-HER2(–) 67% (6 cases), luminal-HER2(+) 22% (2 cases), and HER2 type 11% (1 case). Metastatic sites were bone (78%), pleura (22%), liver (22%) and others (22%). Eribulin was administrated as the first, second, third, and fifth line systemic treatment for metastatic disease in 33%, 22%, 33%, and 11% of patients, respectively. Clinical benefits, i.e. partial response (PR) and stable disease lasting longer than 3 months, were obtained in 3 and 2 patients, respectively, while 3 patients are awaiting evaluation. All patients except one have maintained treatment effects, to date. One patient was switched to another systemic treatment because she developed central nervous system metastasis, detected just one week after the first Eribulin administration. CTCs were detected in all 9 patients and the median number of CTCs was 2.5 (range 1–6) per 10 ml. Two patients had mesenchymal CTCs and both showed PR to the treatment. Moreover, in one of the two patients, mesenchymal CTCs disappeared in three months.

Discussion: Our data suggest that mesenchymal CTC determination might be a good tool for predicting Eribulin responsiveness, although the number of samples is still too small for drawing firm conclusions. The relationship between CTC numbers and chemo-effects must be assessed in future studies. We are currently accumulating more patients and plan to analyse CTC changes during the treatment of individual patients.