Clinical relevance of CK+/CD45+, dual-positive circulating cells (DPCells) in patients with metastatic breast cancer (MBC).

Carolina Reduzzi1, Lorenzo Gerratana2, Youbin Zhang2, Vera Cappelletti1, Maria Grazia Daidone1, Massimo Cristofanilli2
1Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, ITALY, 2Robert H. Lurie Comprehensive Cancer Center, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

*Email address: carolina.reduzzi@northwestern.edu - Telephone contact: +39 3392574483/ +39 0223903054

Background:

The prognostic impact of circulating tumor cells (CTCs) in patients with metastatic breast cancer (MBC) is well recognized. Nonetheless, by using the FDA-approved CellSearch™ platform, CTCs are detected only in a fraction of patients. The presence of circulating cells expressing both epithelial and leukocyte markers (dual-positive cells, DPcells) in cancer patients' blood, has been reported but not investigated. Recently, we demonstrated that DPcells collected from cancer patients’ blood can have an aberrant genome, indicating their tumor origin. Here, we investigated the clinical relevance of circulating DPcells in MBC patients.

Methods:

Blood samples (7.5ml) were collected from MBC patients before starting new therapy and processed with the CellSearch™ platform (Menarini Silicon Biosystems) for CTC and DPcell counting. DPcells were identified as DAPI+ cells, expressing both CK and CD45. The positivity cutoff was ≥1 DPcell/sample.

Results:

Blood samples were collected from patients with luminal (n=72), triple negative (TN, n=30) and HER2+ (n=34) MBC. Fifty-one samples (38%) presented ≥5 CTCs (CTCpos), while 85 (62%) presented <5 CTCs (CTCneg). DPcells were found in 68 patients (50%), either CTCpos/CTCneg (31 and 37 patients, respectively).

DPcells were more frequent than CTCs in patients with HER2+ (59%vs.24%) and TN (53%vs.30%) BC, but not in patients with luminal disease (46%vs.47%).

The association between DPcell/CTC-positivity and survival was assessed in 125 (OS) and 82 (PFS) patients. A significant association between DPcells and PFS was observed: Median PFS= 4.27 vs. 6.70 for DPcellpos and DPcellneg patients, respectively (p=0.046). Interestingly, we observed that among CTCneg patients (n=51), those with DPcells (n=21) experienced a shorter PFS with respect to DPcellneg ones (median PFS= 5.67vs.9.33 months, p=0.041). No difference was observed between median PFS of CTCpos/DPcellpos and CTCpos/DPcellneg patients: 3.57 and 3.63 months, respectively.

Conclusions:

DPcells are detectable in MBC patients, in particular in those subtypes where CTCs are less frequent (HER2+ and TNBC). Moreover, their presence is associated with shorter PFS. These data suggest that DPcells could constitute a new prognostic biomarker in treatment-refractory non-luminal MBC,
especially in CTC<sup>neg</sup> patients. Further studies are needed to validate these preliminary results and better define the clinical validity of this new CTC subpopulation.