Micronuclei in Circulating Stromal Cells Correlated with PD-L1 Expression and Predicts Progression in Metastatic Breast Cancer

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ABSTRACT

Micronuclei (MN) are a result of biological DNA repair mechanisms forming due to internal chromosomal aberrations which indicate sub-clonal cancer populations with higher cell survivability and drug therapy resistance. MN are often observed as small fragments of nucleic acids excised from a primary nucleus in Circulating Stromal Cells (CStCs) as result of DNA damage1,2. CStCs with damaged DNA undergoing repair mechanisms, such as those that form MN, appear to have upregulated expression of programmed cell death ligand (PD-L1). We evaluated CStCs in metastatic breast cancer (mBC) patients for presence of MN and the cell’s PD-L1 expression, to determine its prognostic significance to clinical outcomes.

RESULTS

- MN were identified in CStCs in 59% (n=45/76) of patients.
- MN positive CStCs had a significantly higher PD-L1 expression than MN negative CStCs (p=0.0082), Figure 4.
- Regression analysis identified a significant linear relationship between MN number and PDL-1 expression within CStCs (R²=0.9821, p=0.0089).
- The presence of MN within CStCs was significantly prognostic for worse PFS and worse OS over 24 months (Figures 2 & 3).

CONCLUSIONS

- CStC MN formations in mBC are a type of observable biomarker that can represent an underlying DNA repair mechanism.
- MN formation may represent cellular survivability of sub-clonal cancer populations of more aggressive cancer subtypes which may have worse progression rates.
- Further studies to evaluate the effect of PD-1 immunotherapies in MN positive patients is ongoing.

REFERENCES