Introduction: High expression of secreted protein acidic and rich in cysteine (SPARC) has been associated with poorer overall survival (OS) in patients with resectable PC (Infante. J Clin Oncol. 2007). Among 36 patients with metastatic PC who received nab-P + Gem in a phase I/II study, a higher vs lower level of SPARC was associated with longer OS (median 17.8 vs 8.1 months; \( P < 0.043 \); Von Hoff. J Clin Oncol. 2011). The MPACT trial (N = 861), which revealed superior efficacy for nab-P + Gem vs Gem alone as first-line treatment for metastatic PC (OS, primary endpoint; median 8.5 vs 6.7 months; \( P < 0.001 \); Von Hoff. N Engl J Med. 2013), investigated the relationship between SPARC and clinical outcomes as an exploratory endpoint, using a standardized clinical trial assay for SPARC (Illei. USCAP 2013).

Methods: SPARC in stromal fibroblasts and tumor epithelia was evaluated by immunohistochemical (IHC) staining on archival tissue, primarily from metastatic lesions, with the ON1-1 anti-SPARC monoclonal antibody (Invitrogen) and scored by 2 blinded pathologists. Stromal SPARC was scored as high (\( \geq 50\% \) of fibroblasts stained) or low (\(< 50\% \) of fibroblasts stained). Tumor SPARC was scored using a histoscore (0 = negative; < 100 = low; \( \geq 100 \) = high). Plasma SPARC was determined by ELISA in samples collected at baseline and every 8 weeks. Multivariate analyses were conducted using a stepwise procedure.

Results: Stromal SPARC was evaluable in 30% of patients (131 for nab-P + Gem; 125 for Gem alone). The MPACT clinical trial SPARC IHC assay exhibited 86% concordance with the assay used in the phase I/II study (comparison performed on 22 patient samples from the phI/II study). However, in the MPACT trial, stromal SPARC expression (high [n = 71] vs low [n = 185]) was not associated with OS (HR 1.019; \( P = 0.903 \)). A multivariate analysis revealed that treatment, Karnofsky performance status, and presence of liver metastases were significant independent predictors of OS, but stromal SPARC was not. Tumor epithelial SPARC was low or negative in the majority of samples and was not associated with OS. Baseline plasma SPARC was evaluable in 40% of patients (188 for nab-P + Gem; 155 for Gem alone). There was no correlation between baseline plasma SPARC and SPARC IHC in archival tumor tissues. Furthermore, a Cox regression model revealed that neither baseline plasma SPARC nor change from baseline were significant independent predictors of OS. In addition, stromal, tumor epithelial, and plasma SPARC failed to show any significant associations with progression-free survival or overall response rate.

Conclusion: In the phase III MPACT trial of patients with metastatic PC, SPARC level was neither prognostic for OS nor predictive of response to treatment. The body of evidence suggests that it is premature to recommend treatment decisions for patients with metastatic PC based on SPARC expression in stroma, tumor epithelia, or plasma.

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