The prevalence of CD146 expression in breast cancer subtypes and its relation to outcome

JE de Kruiff1, AM Timmermans1, MA den Bakker2, AMC Trapman3, R. Foekens1, E Oomen-De Hoop1, M. Smid1, A. TjonA Fat - Hollestelle1, CHM van Deurzen2, ME Meijer - van Gelder1, J.A. Foekens1, JW. Martens1, S. Sleijfer2
1Department of Medical Oncology and Cancer Genomics Netherlands, Erasmus MC Cancer Institute, Rotterdam, Netherlands; 2Department of Pathology, Erasmus MC Cancer Institute, Rotterdam, Netherlands

Background: CD146 has several putative (patho)physiological roles in breast cancer. The most prominent is its involvement in the induction of epithelial-to-mesenchymal transition, which might have an effect on cancer phenotype and aggressiveness. Here, we investigated the prevalence of CD146 expression and its prognostic role in breast cancer subtypes.

Methods: In total, 1,025 breast cancer patients were available for this retrospective study. From all patients, formalin-fixed paraffin-embedded primary breast cancer tissue was collected and embedded in tissue microarrays, which were stained for CD146. CD146 expression was defined as > 1% of the tumor cells showing CD146 membrane staining. Clinical data were available from all patients (median follow up 118 months, range 4-120). For subtype analysis the Pearson chi-square test was used and the Cox proportional hazards model for survival analyses. Only patients who were lymph node negative and did not receive (neo)adjuvant systemic treatment were included in the survival analyses (n = 551).

Results: 113 (11%) out of 1,025 tumors showed CD146 expression. Of these, 43% of the tumors had > 50% of the tumor cells showing CD146 membrane staining. From the molecular subtypes, CD146 positive tumors are often of the triple negative subtype (76 out of 119 (64%), p < 0.001) and histologically of the medullary type (11 out of 23 (48%), p < 0.001). In univariable analysis, CD146 was a prognostic factor for both poor metastasis-free survival (MFS) and overall survival (OS) (respectively HR 1.65, 95% CI 1.02-2.66, p = 0.041 and HR 1.66, 95% CI 1.03-2.69, p = 0.037). When correcting for the traditional prognostic factors (including age, tumor size and grade, ER, PR and HER2) in multivariable analysis, CD146 was not an independent prognostic factor for MFS and OS (respectively HR 1.63, 95% CI 0.93-2.87, p = 0.088 and HR 1.46, 95% CI 0.82-2.61, p = 0.197).

Conclusions: CD146 protein expression is present in 11% of the primary breast cancer tumors and is most prevalent in the triple negative and medullary subtypes. CD146 is a prognostic factor for MFS and OS in breast cancer patients, but it is not independent of the traditional prognostic factors. Its potential impact on outcome to systemic treatment such as endocrine therapy, remains to be established.

Legal entity responsible for the study: Erasmus University Medical Center

Funding: None

Disclosure: All authors have declared no conflicts of interest.