



AB141. Novel clinical roles for junctional adhesion molecule—a in breast cancer progression

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Background: Junctional Adhesion Molecule-A (JAM-A) has important physiological functions in epithelial and endothelial barriers, but its overexpression has also been linked with tumour progression and poor prognosis in various malignancies. Since JAM-A can be enzymatically cleaved (“cJAM-A”) and has been detected in the bloodstream, we hypothesized that cJAM-A shed from tumours overexpressing JAM-A may represent a possible predictor of treatment resistance in breast cancer.

Methods: An assay was optimised to detect cJAM-A in serum/plasma. Samples were obtained from HER2-positive breast cancer patients (n=20) in Beaumont Hospital. Independently, serial samples were obtained from a diverse

international cohort of breast cancer patients (n=53). Separately, a semi-in vivo chick embryo xenograft model was used to evaluate a novel potential role for JAM-A overexpression and cleavage in driving tumour progression. **Results:** Serum cJAM-A levels in therapy-resistant patients was significantly higher than those in treatment-sensitive patients ($P<0.05$) in an Irish cohort. Semi-in vivo work showed a macroscopic increase in tumour growth in xenograft tumours either over-expressing JAM-A or treated with cleaved JAM-A. Correspondingly, pharmacological inhibition of JAM-A cleavage reduced gross tumour size and histological evidence of tumour invasiveness.

Conclusions: Our data suggest that cJAM-A merits further investigation as a novel biomarker enabling prospective identification of patients at greatest risk of developing therapeutic resistance. We are in the process of expanding this work in a large cohort of serially-sampled breast cancer patients from an international site.

Keywords: Adhesion molecules; biomarkers; breast cancer; xenograft

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