LGI1 mimetic peptide as a directed therapeutic strategy for endocrine related tumour metastasis

RCSI UNIVERSITY OF MEDICINE AND HEALTH SCIENCES

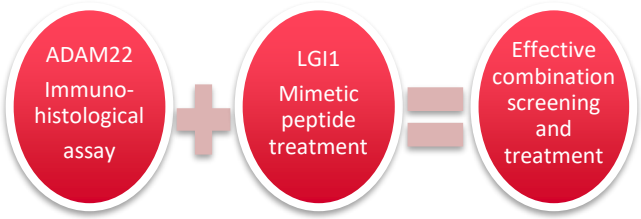
Researchers in RCSI have developed a complete solution for patients suffering from metastatic breast cancer. This technology consists of a commercially ready assay for the detection of ADAM22 in breast cancer tissue and further comprises of a peptide drug based on its natural ligand, LGI1. The combination of this novel peptide drug supplemented with a companion diagnostic has the potential to address the current unmet need of a treatment for endocrine resistant metastatic breast cancer.

BACKGROUND

Endocrine therapy is the treatment of choice for estrogen receptor (ER) positive breast cancer. Approximately 40% of patients eventually relapse and many develop distant metastatic disease. Metastasis is the prime cause of breast cancer patient mortality. There is currently no specific therapeutic for the treatment of endocrine resistant breast cancer.

VALUE PROPOSITION

Researchers in RCSI have identified ADAM22 as a novel therapeutic target for metastatic disease and have manufactured a truncated peptide drug based on its natural ligand, LGI1, to act as an inhibitor. The resultant package is a complete solution for endocrine positive patients with recurrent disease consisting of an immunohistochemical assay to assess metastatic potential followed by a treatment to reduce migration and metastasis. The combination of an LGI1 mimetic peptide therapy, with its receptor ADAM22 acting as a companion diagnostic, has the potential to address the current unmet need of a treatment for endocrine resistant metastatic breast cancer.



TECHNOLOGY

ADAM22 is a transmembrane glycoprotein which plays a role in cancer cell adhesion, dedifferentiation and migration. An immunohistochemical assay for the detection of ADAM22 in primary breast cancer patient tissue has been developed to CLIA/Industry standards. The ability of ADAM22 to predict response to endocrine treatment was assessed in a large cohort of patients whereby ADAM22 expression was significantly associated with reduced disease-free survival in endocrine treated breast cancer patients (Fig. 1).

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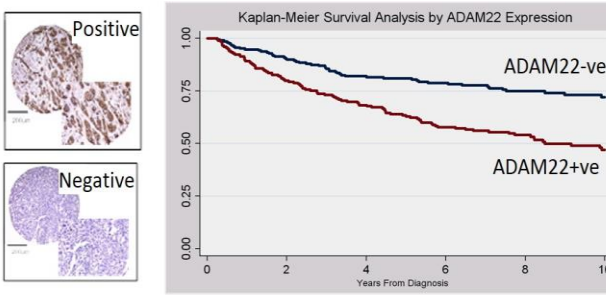

Fig 1. ADAM22 positive expression in primary tumours predicts poor disease-free survival in breast cancer (p<0.0001)

The neuronal protein LGI1 is a specific extracellular ligand for ADAM22. It is a tumour suppressor of glioblastoma and neuroblastoma. The lead peptide reduces metastatic potential of endocrine resistant cells. In *in vivo* studies, treatment of endocrine resistant xenografts with the LGI1 mimetic reduces local disease recurrence and eliminates distant metastatic disease (Fig. 2).

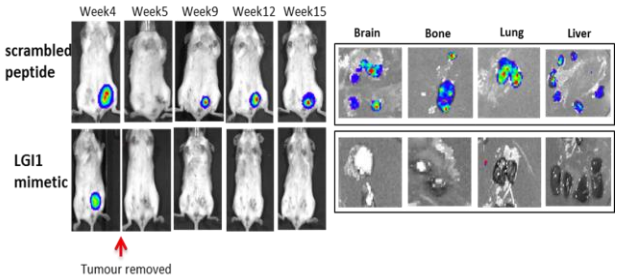

Fig 2. Treatment of endocrine resistant xenograft with LGI1 reduces primary tumour burden and eliminates metastatic disease.

FEATURES	BENEFITS
ADAM22 CLIA-validated commercially ready assay	Predictive test for metastatic potential of breast tumours
LGI1 mimetic peptide	Novel breast cancer therapeutic
Treatment and companion diagnostic	Complete solution for ER positive metastatic breast cancer

TECHNOLOGY READINESS LEVEL

- Patents granted in Europe and the US

REFERENCES

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2. Charmsaz S, Doherty B, Cocchiglia S, et al. ADAM22/LGI1 complex as a new actionable target for breast cancer brain metastasis. BMC Med. 2020;18(1):349. doi:10.1186/s12916-020-01806-4

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