A Prospective longitudinal study of circulating serum progranulin (PGRN/GP88) levels and its association with tumor response to therapies in patients with metastatic breast cancer (MBC) malignancies

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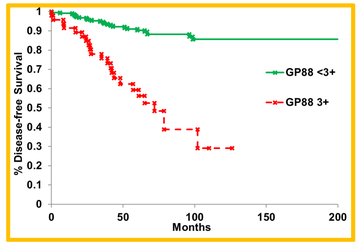
BACKGROUND

Background Rationale

GP88/PGRN , a survival factor overexpressed in breast and lung cancer

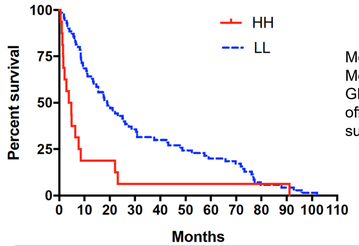
Our laboratory demonstrated GP88's role as an autocrine growth and survival factor in several cancers including breast cancer (BC) and non small cell lung carcinoma (NSCLC): 1) in ER$^+$BC cells, GP88 stimulates proliferation, and confers resistance to anti-estrogen and aromatase inhibitors; 2) GP88 is expressed in 80% invasive ductal carcinoma and is negative in normal mammary tissue; 3) GP88 tumor expression is a prognostic indicator of recurrence and death in BC and NSCLC patients; 4) GP88 serum level in metastatic breast cancer (MBC) and lung cancer patients is increased compared to healthy subjects; 5) Elevated GP88 serum level in MBC patients is associated with disease progression. 5) A retrospective study measuring serum GP88 level with disease status based on RECIST 1.1 criteria has shown that serum GP88 is associated with therapy response and disease progression in MBC patients and improves the performance characteristics of CA15-3 in the standard of care.. These results make GP88 an ideal cancer therapeutic and diagnostic target. A prospective study to measure serum GP88 level in MBC patients was.established and presented here.

Tissue GP88 – Predicts Recurrence



The prognostic value of GP88 expression for disease-free and overall survivals was examined by IHC with formalin-fixed paraffin-embedded tumor biopsies. Kaplan Meier and CPH analysis established that high GP88 score (GP88 = 3+) in IDC was associated with a 5-fold increase in recurrence (4).

Serum GP88 associated with poor outcome



Median survival LL group 20.7 months
Median survival HH group 4.8 months
GP88 level can ne selected as a cut-off level for stratification of patients for survival outcomes

Anti-GP88 AG01 in Phase 1 Clinical study

Category	Item	Status
Research	Demonstrated role of GP88 in cancer, development AG01 mAb	Completed
Product Development	Developed CHO cell line secreting anti-GP88 (AG01) at 2gm/L	Completed
Product Development	Master and working cell bank development and qualification	Completed
Product Development	Designed & validated manufacturing process & formulation AG01	Completed
Product Development	Manufactured 2 x 200gm AG1 for pre-clinical and Tox Studies	Completed
Product Development	Real time stability studies at 2 years	Completed
Pre-Clinical	Demonstrated AG-01 efficacy in several xenograft models	Completed
Pre-Clinical	Completed Acute and Repeat Dose Tox/Pharm in NH Primates	Completed
Clinical Development	Developed and validated tissue /blood assays to measure GP88	Completed
Clinical	IRB approval of the clinical protocol	Completed
Clinical	Manufacture GMP grade AG1 for Phase1A/B Study	Completed
Clinical	Fill finish	Completed
Clinical	Stability studies of Drug product	On-going
Clinical	IND application FDA cleared	Completed
Clinical	Phase 1 Dose escalation of AG01 to define MTD/OBD	On-going

STUDY DESIGN

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An IRB approved, prospective study was established at the UMGCCC to examine serum PGRN/GP88 levels in association with disease status as measured by RECIST 1.1 criteria in MBC pts receiving SOC therapies.

A total of 103 MBC pts with measurable or evaluable metastatic disease will be consented & enrolled. Pts must have been re-staged within 4 wks of study entry & continue or begin new anticancer therapy.

Blood samples are collected every 2-3 mos or if there is a disease event such as clinical or imaging progression.

SOC laboratory assessments & radiographic imaging will be done on study to complement blood collection to measure PGRN/GP88

Primary Objective

To identify if there is a statistically significant change in serum GP88 levels associated with time to progression (TTP) of breast cancer as measured by RECIST 1.1 criteria in MBC pts starting new anticancer therapy or who were staged recently and are planned for further anticancer systemic therapy.

Secondary Objectives

ORR PFS, TTP, TTF in pts receiving SOC therapies
GP88 vs other blood biomarkers (Ca15-3, or Ca 27-29)
GP88 expression in archived tumor tissue from SOC biopsies before/after anticancer treatments in pts with MBC receiving SOC anticancer therapy.

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The samples are stored at -70C until evaluation of PGRN/GP88 using an enzyme linked immunoassay developed by A&G Pharmaceutical.

The serum PGRN/GP88 levels will then be correlated with disease response by RECIST 1.1 (progression, stable for < 6 vs >=6 months, partial/complete response), progression free survival (PFS), duration of response (DOR) and/or need for change of therapy.

In this study the decision about the change of cancer therapy will be based on the SOC approaches & I not guided by PGRN/GP88 results.

As of 11/15/2025
52 subjects signed informed consent for the study. 545 samples have been collected.

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This study is supported by R44CA210817 & the University of Maryland Comprehensive Greenebaum Cancer Center.
PS5-09-03; 12/12/2025, ABS-1786

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