Evaluation of the prognostic value of innate immunity-related biomarkers in early breast cancer (BC)

V. Martini[1,2], F. D'Avanzo[1,3], F. Platini[1,3], M. Allesina[1], F. Favero[1], D. Corà[1], A. Rua[1], C. Saggia[1,3], V. Rossi[1,3], F.M. Varughese[1,2], P.M. Maggiora[1,2], D. Ferrante[1], R. Boldorini[1,3], A. Gennari[1,2,3].

[1]University of Eastern Piedmont, Department of Translational Medicine, DIMET, Novara, Italy; [2]Center for Translational Research on Autoimmune & Allergic Diseases – CAAD; [3]Azienda Ospedaliera Universitaria "Maggiore della Carità", Novara, Italy;

BACKGROUND

CD47 and SIRPα (signal-regulatory protein) are tumor biomarkers of innate immunity, expressed on cancer cells and tumor associated macrophages (TAMs); their interaction provides a "don't eat me" signal that impairs phagocytosis.

The relationship between CD47/SIRPα expression and BC aggressiveness has been investigated, however, its prognostic role is not clarified.

OBJECTIVES

→ To evaluate the expression and the prognostic value of different biomarkers related to innate immunity, in brast cancer, by using public available gene expression datasets and IHC analyses on a retrospective series of patients

→ To assess if double immune co-targeting (i.e. innate and adaptive) might represent a strategy to optimize immunotherapy in BC patients.

METHODS

To verify our hypothesis, we first used in silico data from GOBO and GEPIA, two publicly available datasets: GOBO is a public repository containing microarray data (Affymetrix U133A) from 1881 early BC patients. GEPIA is a web server for analysing RNA expression data of tumours and normal samples from the TCGA and the GTEx projects, by a standard processing pipeline.

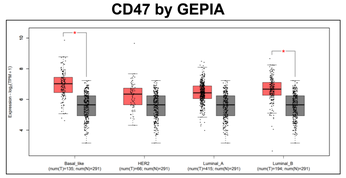
The association between CD47 and SIRPα expression levels and outcome was evaluated using the χ2 test. Disease free survival (DFS) and overall survival (OS) were estimated by Kaplan–Meier life table method.

RESULTS

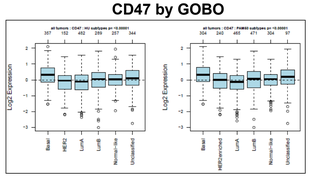
Patients	N (%)
Triple Negative BC	52 (49.5%)
4 years DFS % (95% CI)	69.6% (49.5%-82.9%)
4 years OS % (95% CI)	76.5% (57.6%-87.8%)
ER+/HER2-	53 (50.5%)
10 years DFS % (95% CI)	71.95% (95% IC 66%-76%).
10 years OS % (95% CI)	68% (95% IC 63%-73%)

In silico data showed that CD47 is preferentially expressed in TNBC, as compared to other BC subtypes (p< 0.0001).

CD47 by GEPIA

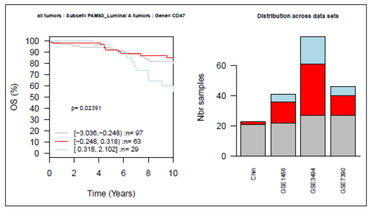


CD47 by GOBO



CD47 upregulation is associated to a worse OS in Luminal A BC.

(GOBO p<0.001, n= 189 patients).



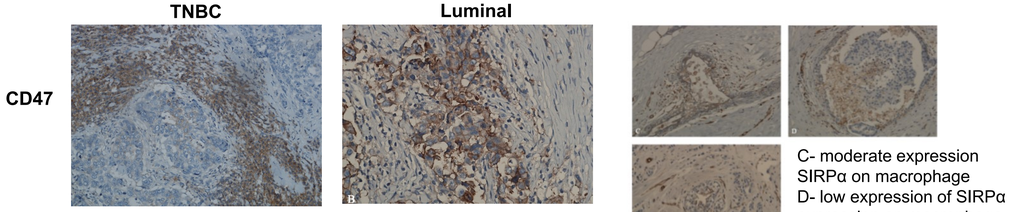
→ CD47 high-expression

→ CD47 intermediate-expression

→ CD47 low-expression

By IHC analysis in our retrospective series, CD47 was overexpressed in 80% of TNBC and in 56% of Luminal BC samples.

SIRPα was expressed in 20% of TAMs and in 50% of TN BC samples.



C- moderate expression SIRPα on macrophage
D- low expression of SIRPα expression on macrophage
E- SIRPα expression on tumour cells and on vessels

Expression of CD47 and SIRPα on tumour cells and on macrophage on BC

Triple Negative BC, N (%)	CD47 N (%)	SIRPα tumour N (%)	SIRPα macrophages N (%)
52 (100%)	44 (84.6%)	24 (46%)	7 (13.5%)

ER+/HER2-, N (%)	CD47 N (%)	SIRPα tumour N (%)	SIRPα macrophages N (%)
53 (100%)	30 (56,6%)	8 (15%)	6 (11%)

CONCLUSIONS

Biomarkers of innate immunity are differently expressed across BC subtypes and seem to be useful to characterize different subtypes.

REFERENCES

1. Schmid P, et al. N Engl J Med. 2018;379:2108–21,
2. Green DR, et al. Nat Rev Immunol. 2009;9:353–63,
3. *Willingham SB. Et al. Proc Natl Acad Sci. 2012;109:6662–7.*