The clinical actionability of PTEN protein and gene expression analysis in HR- and HER2+ breast cancers

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ESMO BREAST CANCER VIRTUAL CONGRESS

ePoster #10P

BACKGROUND

- Phosphatase and tensin homolog (PTEN) is a tumor suppressor with a key role in breast cancer tumorigenesis, tumor progression, and resistance to therapy.
- The clinical value and reliability of PTEN testing in breast cancer is still unclear.

AIM OF THE STUDY

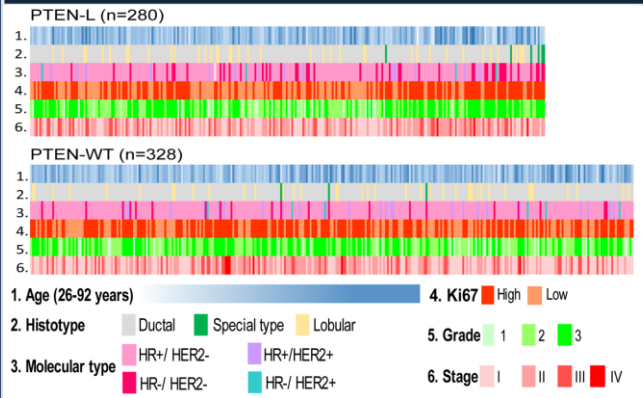
Proof-of-principle study to identify high-risk breast cancers based on the relationship between PTEN and other biomarkers

METHODS

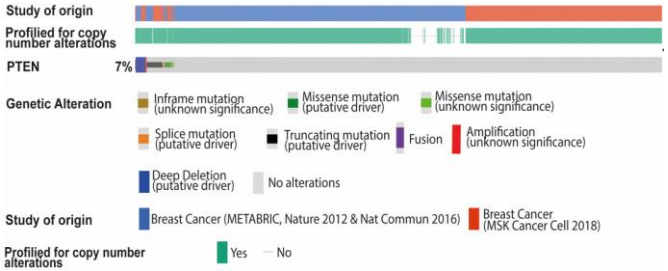
- 608 breast cancers were subjected to PTEN expression analysis by IHC, scored using a three-tired system, and clustered in PTEN-low (PTEN-L) - scores 0/1 - and PTEN-retained (PTEN-WT) - score 2.
- Clinical and genomic data of 4,265 breast cancers were extracted from cBioPortal (METABRIC & MSK).
- Fisher's and Chi-squared tests, Odds ration and 95% CI were calculated for each variable; multinomial logistic regression models and survival analyses were performed.

RESULTS

1. Frequency of PTEN protein loss is higher than mutations



Decreased or null expression of PTEN protein was found in 280 (46.1%) breast cancers



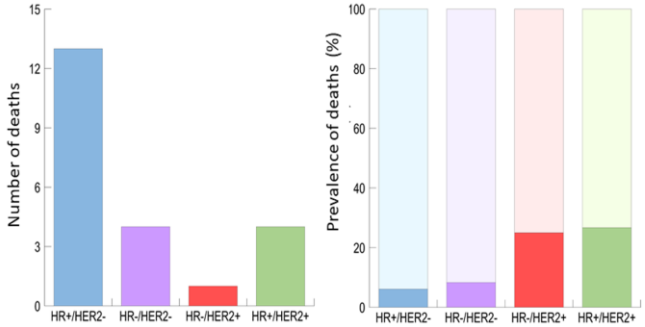
Genetic alterations in PTEN were found in 315 (7.4%) of patients

2. Heterogeneous prevalence of PTEN alterations

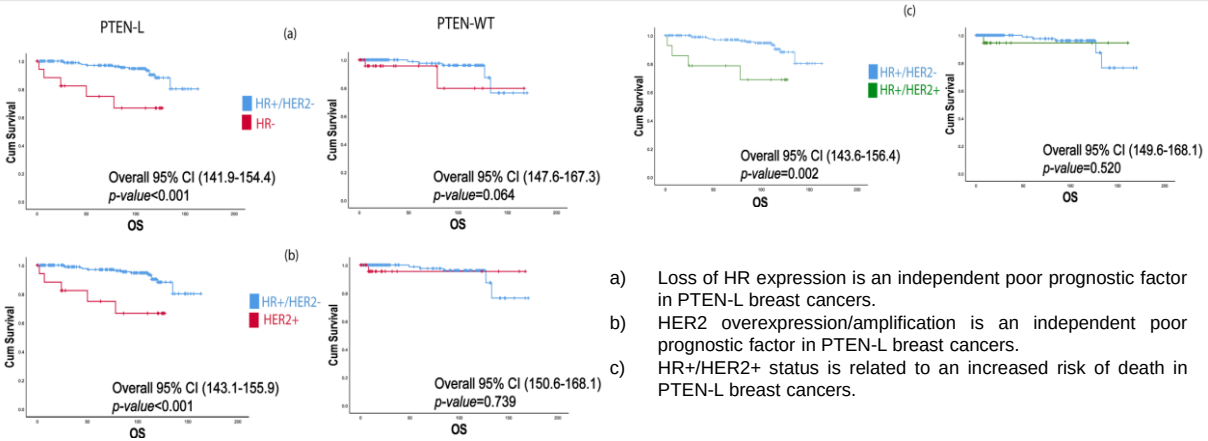
	PTEN-L	PTEN-WT	*p*-value
All patients, n (%)	280 (46.1)	328 (53.9)	
HR and HER2 status, n (%)			
HR+/ HER2-	213 (76.1)	275 (83.8)	0.0008
HR-/ HER2+	4 (1.4)	6 (1,8)	
HR+/ HER2+	15 (5.4)	25 (7.6)	
HR-/ HER2-	48 (17.1)	22 (6.7)	

Higher frequency of triple-negativity in PTEN-L breast cancers than in PTEN-WT

3. Higher death rates in PTEN-L HER2+ breast cancers



4. PTEN analysis is able to identify prognostically relevant subsets of breast cancers



a) Loss of HR expression is an independent poor prognostic factor in PTEN-L breast cancers.

b) HER2 overexpression/amplification is an independent poor prognostic factor in PTEN-L breast cancers.

c) HR+/HER2+ status is related to an increased risk of death in PTEN-L breast cancers.

CONCLUSIONS

- The analysis of PTEN status may provide additional data to perform a tailored risk assessment of patients with HR- and HER2+ breast cancers.
- Future studies on the post-transcriptional mechanisms of PTEN may explain the diverse frequency between PTEN protein and gene alterations.

Selected bibliography: Masson et al. Cold Spring Harb Perspect Med 2020; Lopez et al. Int J Mol Sci 2020; Fusco et al. Front Oncol 2021; Kingston et al. JCO Precision Oncology 2019

Conflict of interests: NF has received honoraria from MSD, Boehringer Ingelheim, Novartis; EGR from ThermoFisher, Roche, Novartis, AstraZeneca, outside this work. All other authors declare no potential conflicts of interest.

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