Detection of germline and somatic pathogenic variants in patients with de novo metastatic breast cancer (dnMBC) and assessment of their prognostic relevance: A Hellenic Cooperative Oncology Group (HeCOG) translational cohort study

Poster
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Introduction

- De novo metastatic breast cancer (dnMBC) remains a clinical challenge
- The incidence of dnMBC is approximately 5–6%
  dnMBC is associated with distinct clinicopathological features and possibly with an improved prognosis
  the biological and genomic characteristics of dnMBC remain largely unexplored
- Since dnMBC is treatment-naïve by definition, it presents an ideal model for investigation of primary tumor biology

Aim

- Explore the prevalence and clinical value of genomic and genetic features in patients with dnMBC

Methods and Materials

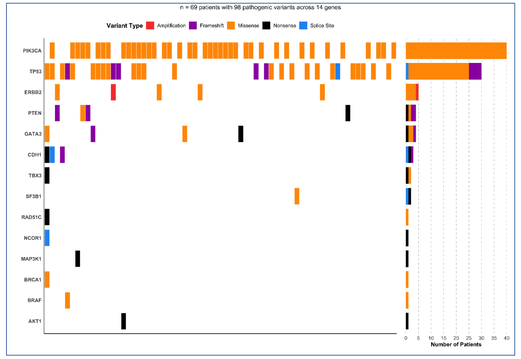
- Retrospective & prospective study conducted on biological samples from 106 patients with dnMBC
- Patients treated at HeCOG-affiliated Departments of Oncology
- Tumor tissue was collected from either the primary tumor or an accessible metastatic lesion. Peripheral blood samples were also collected
- Next-generation sequencing (NGS) was performed on Ion Torrent PGM and S5 Prime platforms

Results

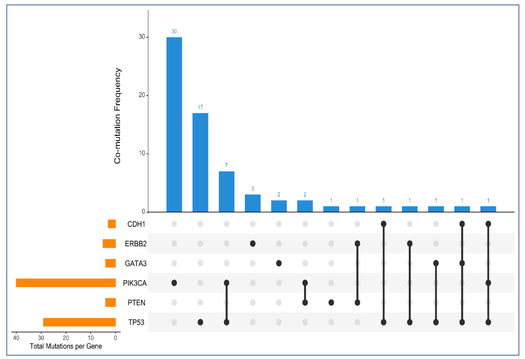
Table 1. Patient and Treatment Characteristics

	Overall N (%)
Menopausal Status	
Peri/Premenopausal	36 (34.0%)
Postmenopausal	69 (65.1%)
Family history of cancer	
No	76 (71.7%)
Yes	30 (28.3%)
Performance status	
0	77 (72.6%)
1	23 (21.7%)
2	5 (4.7%)
3	1 (0.9%)
Surgery type	
Biopsy only	64 (60.4%)
MRM/SM/PM	42 (39.6%)
# of organ systems involved	
1	11 (10.4%)
2-3	84 (79.2%)
>3	11 (10.4%)
Histological type	
Ductal	79 (74.5%)
Lobular	13 (12.3%)
Mixed	5 (4.7%)
Other	9 (8.5%)
Histological grade	
I	3 (2.8%)
II	50 (47.2%)
III	52 (49.1%)
Ki-67 index	
<20	21 (19.8%)
>=20	58 (54.7%)
Subtype	
HR+/HER2-	66
HER2 positive	35
TNBC	5

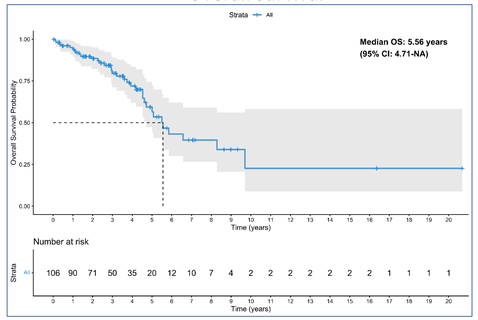
Genomic landscape of dnMBC



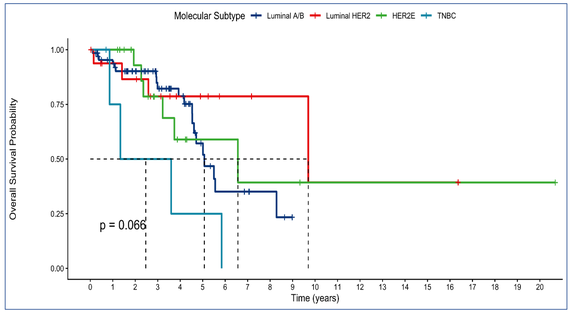
Gene co-mutation patterns



Overall survival



Overall survival among subtypes



Subtype	N	Events	Median OS (years) 95% CI	3-Year OS 95% CI	5-Year OS 95% CI
ER/PgR+/HER2-	66	20	5.07 (4.62-NR)	82.2% (71.9-94%)	57.2% (41.3-79.2%)
HER2+	35	10	9.7 (6.57-NR)	78.7% (64.8-95.5%)	68.5% (52.1-90%)
TNBC	5	4	2.47 (0.86-NR)	50% (18.8-100%)	25% (4.6-100%)

At least one PV was present in 69 of 106 tumors (65.1%), with most carrying PVs in PIK3CA (40 cases; 37.7 %) and TP53 (29 cases; 27.4 %). Recurrent, albeit less frequent, PVs were also observed in ERBB2, GATA3, PTEN, CDH1 and AKT1 (each present in ≥ 2 tumors). Meanwhile, germline sequencing revealed single PVs in two patients, one in TP53 and the other in PTEN.

Having more than 3 organ systems involved as well as TNBC phenotype were significant negative predictors for survival.

Conclusions

This comprehensive analysis of clinical and genomic biomarkers in de novo metastatic breast cancer provides important prognostic information and highlights the genomic heterogeneity of this disease. Integration of clinical and molecular features may improve risk stratification and guide personalized treatment strategies.

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