Is genetic testing of HER2-negative metastatic breast cancer patients implemented into clinical practice?

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#1402

Abstract

Purpose
Genetic testing in HER2-negative (HER2-) metastatic breast cancer (mBC) is necessary to allow optimal treatment including PARP inhibitors. The present study evaluated the implementation of genetic testing in a real-world setting to reveal and subsequently allow targeting of potential inadequacies and risk factors for low testing frequency.

Methods
We performed a retrospective analysis including HER2- mBC patients treated at a single academic center starting from 10.4.2019 (date of EMA approval of Olaparib for gBRCAmut HER2- mBC). The primary objective of the study was to evaluate the rate of HER2- mBC patients that were recommended to undergo genetic testing by the multidisciplinary tumor board (MTB). The secondary objective was to identify factors that were associated with a higher likelihood of having undergone genetic testing.

Results
47.6% (109 of 229) of HER2- mBC patients had been recommended to undergo genetic testing by the MTB. Of these informed patients, 89.0% (97 of 109) underwent genetic testing, of which 11.6% (11 of 95) had a BRCA mutation and were eligible for PARPi treatment. In multivariate analysis younger age (p-value: 0.0007), HR+/HER2- subtype (p-value < 0.0001) and positive family history for breast and ovarian cancer (p-value: 0.0001) were significantly associated with the performance of genetic counseling.

Conclusion
The present study demonstrated low genetic counseling rates of HER2- mBC patients especially in patients without specific risk factors for hereditary breast cancer. Informed patients showed a high willingness to undergo genetic testing. Genetic testing revealed targetable mutations in over 10% of tested patients.

Keywords
Genetic testing, HER2- metastatic breast cancer, PARP inhibitor, platinum salt

Introduction

- two pivotal trials OlympiAD and EMBRACA demonstrated a significantly longer median progression free survival (PFS) with the PARPis Olaparib and Talazoparib versus treatment of physicians choice (TPC) with consistent results across various subgroups (OlympiAD: median PFS 7 months versus 4.2 months, hazard ratio [HR] for disease progression or death, 0.58 [95%CI, 0.43 to 0.80]; p < .001; EMBRACA: median PFS 8.6months versus 5.6 months, HR for disease progression or death,0,54[95%CI,0.41 to 0.71], p < .001) *(1,2)*
- Up to 10% of patients with metastatic HER2-negative (HER2-) breast cancer (BC) have a BRCA mutation with an even higher prevalence (>30%) in triple negative (TN) disease and are therefore eligible for PARPi treatment *(3)*
- Notably, more patients with a gBRCA mutation have hormone receptor positive (HR+), HER2- disease as this subtype is more prevalent compared to TNBC

Introduction cont.

- Given the advent of platinum salts as well as PARPi in BRCA-associated HER2- mBC timely genetic testing in these patients is of high importance to allow adequate treatment *(4)*
- Yet, testing rates in these patients have been reported suboptimal varying between 16.7% to 97% *(5,6)*

Aim fo the Study

The present study evaluated the implementation of genetic testing in a real-world academic setting in order to uncover and subsequently allow targeting of potential deficiencies as well as risk factors that are associated with a lower testing rate .

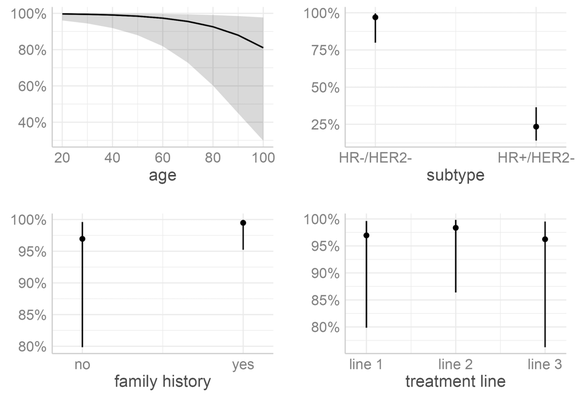
Methods and Materials

- included all HER2neg mBC patients treated at the Department of Obstetrics and Gynecology of the Medical University of Vienna, Austria, starting from 10.4.2019 (date of EMA approval of Olaparib for gBRCAmut HER2- mBC)
- retrospective chart review and assessed whether genetic counseling was recommended by the MTB and testing was subsequently performed, as well as patient and disease characteristics
- In the course of genetic testing 18 genes including ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11 and TP53 were evaluated using next-generation sequencing (NGS)
- Statistical analysis was done using R version 4.3.2 and package viridis v0.6.4. Categorical data are presented by absolute and relative frequencies, whereas numerical data are aggregated by mean and standard deviation. Differences between groups were tested with Chi squared test for the former and Student's t-test for the latter
- 'Genetic testing: yes/no' was modeled by logistic regression with age, HR+/HER2- subtype, family history and treatment line as independent variables. A p-value below 0.05 is viewed as statistically significant

Results

- 229 patients with a HER2- mBC were included in the study. The mean age of the study population was 64 ± 13 years
- 76.4% (175 of 229) of patients had a HR+, HER2- mBC and 23.6% (54 of 229) of patients a TN subtype. Patients were on average on the second treatment line for the metastatic disease at the time of study inclusion (mean 2.0 ± 1.5)
- 47.6% (109 of 229) of HER2- mBC patients had been advised to undergo genetic testing by the MTB. Of these informed patients, 89.0% (97 of 109) underwent genetic testing
- 11.0% (12 of 109) of informed patients did not undergo genetic testing, 2 of these patients refused genetic testing after counseling, 1 patient died prior to genetic testing and in 9 patients the reason for not having undergone genetic testing was not elicit
- In multivariate analysis the variables younger age (p-value: 0.0007), HR+/HER2- subtype (p-value < 0.0001) and positive family history for breast and ovarian cancer (p-value: 0.0001) were significantly associated with the performance of genetic counseling
- Treatment line showed no association with the performance of genetic counseling (p-value 2nd line: 0.2292, p-value 3rd line: 0.68)

influencing factors for testing rates



Results cont.

- 11.6% (11 of 95) of tested patients had a BRCA 1 or 2 mutation and were therefore eligible for PARPi treatment (see table 1)

Table 1 Overview of the genetic test results

Genetic test result	Number of patients (n_{total} = 95)
WT or VUS	80 (84.2%)
BRCA 2 1 patient with a somatic mutation (Only tumor tissue was tested in this patient.)	8 (8.4%)
BRCA 1	4 (4.2%)
PALB 2	1 (1.1%)
CHEK 2	1 (1.1%)

- 75% (9 of 12) of patients with a germline or somatic BRCA mutation had received treatment with a PARPi
- three patients with a gBRCAmut who had not received a PARPi were on an early treatment line for metastatic disease (1 patient with TN disease on 1st TL, 1 patient with HR+ disease on 1st treatment line and 1 patient with HR+ disease on 2nd treatment line)
- 2 HER2- mBC patients without a germline or somatic BRCAmut were treated with a PARPi on the basis of compassionate use as well as in the course of a clinical study

Conclusions

- **The genetic testing rate in HER2- metastatic breast cancer patients was low (48%).**
- **Testing rates were lowest in case of older age, HR+subtype and no family history.**
- **Counseled patients showed a high willingness (89%) to undergo genetic testing.**
- **Genetic testing revealed targetable mutations in over 10% of tested patients.**

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References

1. Robson, M., et al., *Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation.* N Engl J Med, 2017. **377**(6): p. 523-533.
2. Litton, J.K., et al., *Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation.* N Engl J Med, 2018. **379**(8): p. 753-763.
3. Fasching, P.A., et al., *Mutations in BRCA1/2 and Other Panel Genes in Patients With Metastatic Breast Cancer -Association With Patient and Disease Characteristics and Effect on Prognosis.* J Clin Oncol, 2021. **39**(15): p. 1619-1630
4. Tung, N.M. and J.E. Garber, *BRCA1/2 testing: therapeutic implications for breast cancer management.* Br J Cancer, 2018. **119**(2): p. 141-152
5. Tung, N., et al., *Frequency of mutations in individuals with breast cancer referred for BRCA1 and BRCA2 testing using next-generation sequencing with a 25-gene panel.* Cancer, 2015. **121**(1): p. 25-33.
6. Childers, C.P., et al., *National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer.* J Clin Oncol, 2017. **35**(34): p. 3800-3806

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