Germline mutation status and therapy response in high-risk early breast cancer: Results of the GeparOcto study (NCT02125344)

Esther Pohl-Resigno1, Jan Hauke1, Kerstin Rhiem1, Volker Möbus2, Jenny Furlanetto1, Carsten Denkert3, Peter A. Fachinger4, Claus Hanusch5, Hans Tesch1, Nana Weber-Lassalle1, Volkmar Müller6, Michael Untich7, Kristína Libe8, Bianca Lederer9, Christian Jackisch10, Valentina Nekludova1, Rita K. Schmutzler11, Sibylle Loh12, Andreas Schneeweiss7, Eric Hahnen1

1Center for Familial Breast and Ovarian Cancer and Center for Integrated Oncology (CIO), Cologne, Faculty of Medicine, University of Duisburg-Essen, Essen, Germany; 2Department of Obstetrics and Gynecology, Klinikum Frankfurt Nord, Academic Hospital of the Goethe University Frankfurt, Frankfurt, Germany; 3German Breast Group (GBG), Neu-Isenburg, Germany; 4Institut für Pathologie, Philippus-Universität Marburg and Universitätsklinikum Marburg, University Hospital Erlangen, Erlangen, Germany; 5Robustuziklinikum, Frauenklinik, Munich, Germany; 6Hautklinikum Hamburg-Eppendorf, University Medical Center Hamburg, Hamburg, Germany; 7Department of Gynecology and Obstetrics, Hallo Klinikum Berlin-Buch, Berlin, Germany; 8Gütersloher Hirntumorstift, Breast Center, Hannover, Germany; 9Bar region Center for Tumor Diseases, University of Heidelberg and German Cancer Research Center, Heidelberg, Germany.

Abstract 573

GeparOcto compared the efficacy of two neoadjuvant treatment regimens in high-risk breast cancer (BC): Sequential intense dose-dense epirubicin, paclitaxel, and cyclophosphamide (idEEPc) and weekly paclitaxel plus non-neupgylated liposomal doxorubicin (PM), plus carboplatin (PMCb) in triple-negative BC (TNBC) (Figure 1). Overall, there was no difference in pathological complete response (pCR, ypT0is ypN0) rates [1]. Here, we analyzed pCR rates according to germline mutation status.

Figure 1. Study design. Patients with TNBC, high-risk HER2-HR+ BC, or HER2+ BC were randomized to one of the two treatment arms, idEEPc or PMCb.

Results

Background

The next generation sequencing (NGS)-based germline mutation analysis of BRCA1, BRCA2, and 16 further BC (candidate) predisposition genes (ATM, BARD1, BRIP1, CDH1, CHEK2, FANCN, MRE11A, NBN, PALB2, PTEN, RAD50, RAD51C, RAD101, STK11, TP53, XRCC2; no mutation identified) was carried out in 914 patients: 369 patients with TNBC (idEEPc n=194; PMCb n=199), 156 patients with high-risk HER2-HR+ BC (idEEPc n=75; PMCb n=81), and 365 patients with HER2+ BC (idEEPc n=182; PMCb n=183) (Figure 2).

Deletious (International Agency for Research on Cancer (IARC) class 4/5) variants were validated by Sanger sequencing. Detection of copy number variations (CNV) was carried out using an in house CNV detection tool and established open access tools. Validation of pCR rates was performed by other Multiplex Ligation-dependent Probe Amplification (MLPA) or real-time polymerase chain reaction.

Figure 2. Flow diagram.

Patients and Methods

Figure 3. gBRCA1/2 mutation status and pCR rates overall and in subgroups of TNBC, high-risk HER2-HR+, and HER2+ BC.

Figure 4. gBRCA1/2 mutation status and pCR rates overall and in subgroups of TNBC, high-risk HER2-HR+, and HER2+ BC per treatment arm A) idEEPc (n=451) and B) PMCb (n=463).

Conclusions

Patients with gBRCA1/2 mutations showed most benefit from neoadjuvant treatment with highest pCR rates achieved in the gBRCA1/2 TNBC / PMCb group. The role of carboplatin for neoadjuvant treatment of gBRCA1/2 TNBC should be further explored. Mutations in further BC predisposition genes are unlikely to predict therapy response.

References


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