Methods: A 75-year old women with rapidly progressive metastatic TNBC and clinical resistance to anthracyclines, taxanes, capecitabine, pembrolizumab and eribulin was enrolled in a molecular profiling program (PERMED trial, NCT02342158). To identify clinically-actionable gene mutations and putative druggable pathways, a pretreatment biopsy of liver metastatic tissue was obtained and analyzed by whole genome array- CGH (aCGH) and targeted next-generation sequencing (NGS) of 559 cancer genes, along with germline sequencing. Gene copy number aberrations (CNAs) and somatic mutation status that could help therapeutic decision were examined.

Results: No germline BRCA mutation was found. The aCGH analysis showed a genomic instability associated with a BRCAness profile and an HRD score of 19. The CNAs analysis showed a focal homozygous loss of RAD51B/RAD51L1 gene, while NGS identified a somatic mutation of BRCA1. Patient received carboplatin single-agent and developed a durable and almost complete response.

Conclusions: These data strongly suggest that carboplatin may be highly effective in advanced TNBC with no germline BRCA mutation but somatic genomic alterations disrupting DNA repair pathways, supporting precision medicine trials evaluating platinum derivatives in this setting.

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91P A major response to carboplatin in a metastatic triple-negative breast cancer patient with somatic mutation of BRCA1 and RAD51B: When chemotherapy meets precision medicine

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Background: Recent clinical data indicate a higher pathological complete response rate when platinum is added to neoadjuvant chemotherapy in triple-negative breast cancer (TNBC), and favorable outcomes have also been observed in metastatic TNBC patients treated with platinum-based regimen. BC associated with germline BRCA mutations display DNA double-strand break repair defects, which are thought to render them particularly sensitive to DNA repair targeting drugs such as PARP inhibitors and/or platinum analogs. In addition, BRCA1/2 genes promoter methylation, somatic mutation, as well as other genomic alterations in DNA repair genes may also drive homologous recombination-deficiency (HRD) and the so-called “BRCAness” phenotype. Yet, their association with sensitivity to platinum derivatives or PARP inhibitors in BC remains discussed.