involved TP53 (70%), BRCA1 (30%) and MYC, PIK3CA, PTEN and RET (20%). Other gene mutations were less frequent (10%).

In BM specimens, 24 genes were altered, especially for CNVs (amplification). TP53 mutation was the most frequent (70%), with the same rate compared to matched primary samples, while MYC (40%), CCNE1 (20%), and PIK3CA (30%) showed a higher frequency rate. RET mutations were utterly absent in BMs. In BMs specimens, 2 fusion events (KIF5B-SBF2 and ZNF83-BRCA1) were identified.

All in all, no differences were shown between genomic alterations and the histotype, the stage or the previous number of chemotherapy lines.

Conclusion These preliminary results highlight changes in the molecular landscape of BM tissue compared to the matched primary one; nevertheless, further evaluation is needed. A phylogenetic analysis is still ongoing at our center. This more comprehensive evaluation may pave the way toward a more precise understanding of the genetics underneath the development of BM, potentially revealing novel molecular targets and leading to prospective future studies and more personalized treatment.

Disclosures None.

**Abstract #765**

Efficacy of Maintenance with PARPi in Advanced Ovarian Cancer According to the Type of BRCA Mutation

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Introduction/Background Currently, little is known about correlations between the type and location of mutations of the BReast CAncer (BRCA) 1/2 genes and response to Poly (ADP-ribose) polymerase inhibitors (PARPi) in ovarian cancer (OC). Clinical data from PAOLA1 study suggest that patients with mutations in DNA binding domain (DNA-BD) of BRCA1 are more sensitive to the combination of olaparib/bevacizumab and mutations in the DNA-BD of BRCA2 confer excellent outcomes. No data are available on mutation types and PARPi single agent sensitivity.

Methodology This multicenter, retrospective study involved BRCA1/2 mutated high-grade serous OC patients receiving PARPi as maintenance, after first-line, platinum-based chemotherapy. Clinical and survival data were collected from 4 academic centers. Patients were classified according to the mutation type: frameshift, missense, nonsense and splicing. The primary outcome was progression-free survival (PFS) among the different groups. PFS was also analyzed according to the involved functional domain (FD) of BRCA1 (RING, DNA-BD or BRCA1 C terminus [BRCT]) and BRCA2 (PALB2, RAD51-BD; DNA-BD).

Results 140 patients treated between 2018–2022 were included. 81 (57%) and 60 (43%) harbored BRCA1 and BRCA2 mutations, respectively. Overall, 79 (56%) patients presented frameshift mutation, 17 (12%) missense, 36 (25.5%) nonsense and 8 (5.7%) splicing mutation. After a median follow-up of 20 months, patients harboring a missense mutation had 3-yr PFS of 94%, compared with 73% of those with a frameshift mutation (p=0.05) and 75% of those with a nonsense mutation (p=0.065) (figure 1A).

Regarding the FDs, in patients with DNA-BD mutation of BRCA1/2, 3-yr PFS was 91.4%, compared with 88.7% in mutation in the other domains (p=0.64) (figure 1B).

Conclusion In our cohort, missense mutation in the BRCA1/2 genes seems to confer longer PFS than other mutation types. Therefore, mutation type might impact PARPi response. Larger studies are needed to confirm this hypothesis-generating analysis.

Disclosures None.

Abstract #765 Figure 1  PFS according to BRCA mutation type and site.