PARP inhibitors use in patients in germline *PALB2* or somatic *BRCA1/2* mutations carriers with metastatic breast cancer: Real life data from the ESME database

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INTRODUCTION

Poly (ADP-ribose) polymerase inhibitors (PARPi) are approved for the treatment of HER2-negative metastatic breast cancer (MBC) in germline (g)*BRCA1/2* pathogenic alteration (m) carriers.

Olaparib and talazoparib showed although efficacy in MBC patients with somatic (s)*BRCA1/2*m and/or g*PALB2*m in phase 2 trials. In Tung et al.'s trial[a], patients with no more than two chemotherapy and without platinum-refractory disease, the median PFS (mPFS) was 13.2 months and 6.3 months for g*PALB2*m (n=11) and s*BRCA1/2*m (n=16) respectively. Batalini et al.[b] reported a mPFS of 5.4 months for the s*BRCA1/2*m or g*PALB2*m cohort (n=30).

OBJECTIVE: to investigate the effectiveness of PARPi in this setting in the real-life French Epidemiological Strategy and Medical Economics Metastatic Breast Cancer (ESME-MBC) cohort.

MATERIELS & METHODS

ESME-MBC, a nationwide observational cohort, gathers data on MBC patients treated in 18 French Cancer Centers from 2008 on (NCT03275311).
All patients included were treated with PARPi for metastatic disease, after s*BRCA1/2m* or g*PALB2m* identification.

Primary endpoint: progression-free survival (PFS).
Secondary endpoints: overall survival (OS) from treatment initiation, PFS and OS according to type of mutation, type of PARPi and line of treatment.

The Kaplan-Meier method was used to assess survival.

RESULTS

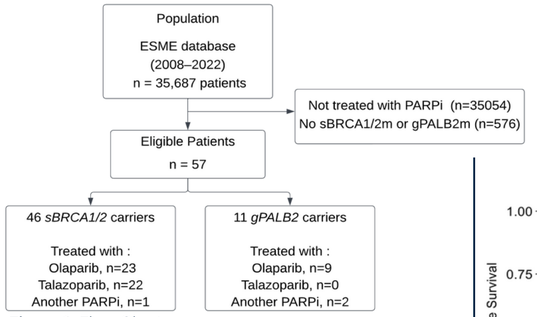


Figure 1. Flow Chart

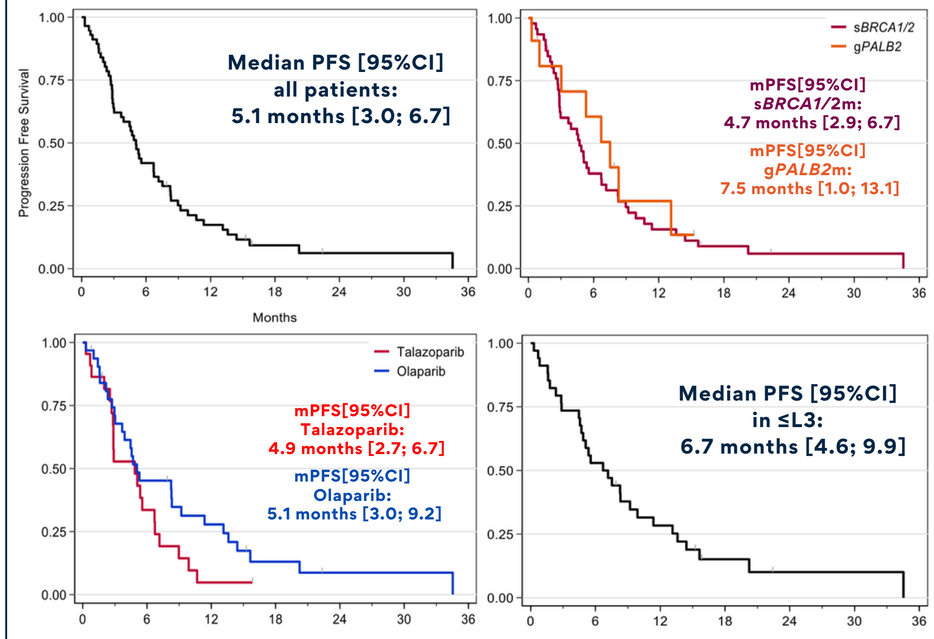
	sBRCA1/2 (%) n=46	gPALB2 (%) n=11
Gender		
Male	1 (2%)	0
Female	45 (98%)	11 (100%)
Age at PARPi initiation	53	60
[range]	[31;83]	[43;79]
HR Status		
Negative	18 (39.1%)	5 (45.5%)
Positive	28 (60.9%)	6 (54.5%)
De novo metastatic		
Yes	22 (47.8%)	5 (45.5%)
No	24 (52.2%)	6 (54.5%)
Type of metastases		
CNS	3 (6.5%)	0
Visceral non-CNS	24 (52.2%)	2 (18.2%)
Non visceral	19 (41.3%)	9 (81.8%)
N° Line of first PARPi		
Median [range]	3 [1;8]	3 [2;10]
≤ Third-line	28 (60.9%)	6 (54.5%)
Fourth or more	18 (39.1%)	5 (45.5%)
Platinum chemotherapy before PARPi		
Yes	11 (23.9%)	4 (36.4%)
No	35 (76.1%)	7 (63.6%)
Clinical trial		
Yes	16 (34.8%)	5 (45.5%)
No	30 (65.2%)	6 (54.5%)
Type of PARPi		
Olaparib	23 (50%)	9 (81.8%)
Talazoparib	22 (47.8%)	0
Another PARPi	1 (2.2%)	2 (18.2%)

Table 1. Patient's characteristic

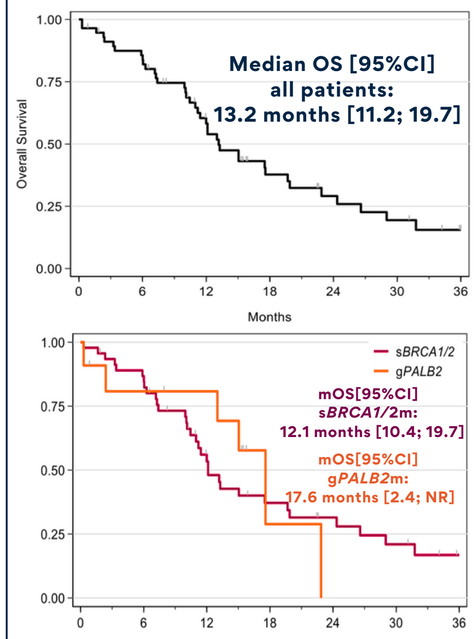
Seven patients received PARPi as first-line treatment; all with a s*BRCA1/2*m and 6 were triple-negative. Three patients with g*PALB2*m received PARPi as second-line treatment, 2 triple-negative and 1 HR-positive/HER2-negative. PARPi was initiated after a maximum of two metastatic chemotherapy regimens (PARPi≤L3) for 34 patients (28 s*BRCA1/2*m; 6 g*PALB2*m), equally split between triple-negative and HR-positive/HER2-negative cases.

Median follow-up was 31.0 months [15.6; 35.7].

Progression-free survival



Overall survival



CONCLUSION

This multicenter real-life cohort with MBC showed PFS comparable to the ones reported in clinical trials with PARPi treatment for s*BRCA1/2*m or g*PALB2*m patients.

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References: [a.] Tung NM, et al. TBCRC 048: Phase II Study of Olaparib for Metastatic Breast Cancer and Mutations in Homologous Recombination-Related Genes. *J Clin Oncol*. 2020;38(36):4274-4282. doi:10.1200/JCO.20.02151

[b.] Batalini F et al. Homologous Recombination Deficiency Landscape of Breast Cancers and Real-World Effectiveness of PARPi in Patients With Somatic *BRCA1/2*, Germline *PALB2*, or Homologous Recombination Deficiency Signature. *JCO Precis Oncol*. 2023;7:e2300091. doi:10.1200/PO.23.00091

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