#260P

ESMO BREAST CANCER
BERLIN GERMANY
15-17 MAY 2024

LUZERN: Phase 2 trial of niraparib and aromatase inhibitors (AI) for pretreated hormone receptor-positive/HER2-negative germline *BRCA*-mutated advanced breast cancer

Salvador Blanch[1], Judith Balmaña[2], Laura Lema[3], José Ángel García-Sáenz[4], Elena Filipovich Vegas[5], Begoña Jiménez[6], Juan de la Haba[7], José Manuel Pérez-García[8,9], Marta Campolier[9], Eileen Shimizu[9], Daniel Alcalá-López[9], Miguel Sampayo-Cordero[9], Javier Cortés[8,9,10], Antonio Llombart-Cussac[9,11]

1. Instituto Valenciano de Oncología, Valencia, Spain 2. Vall d'Hebron University Hospital, Barcelona, Spain 3. Hospital Universitario 12 de Octubre, Madrid, Spain 4. Hospital Clínico San Carlos, Madrid, Spain 5. Complejo Asistencial de Ávila, Ávila, Spain 6. Hospital Universitario Virgen de la Victoria, Málaga, Spain 7. University Hospital Reina Sofia, Córdoba, Spain 8. International Breast Cancer Center (IBCC), Pangaea Group, Quiron Group, Barcelona, Spain 9. Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co, Jersey City (New Jersey, USA), Sao Paulo (Brazil)10. Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain 11. Hospital Universitario Arnau de Vilanova, Universidad Católica de Valencia, Valencia, Spain

BACKGROUND

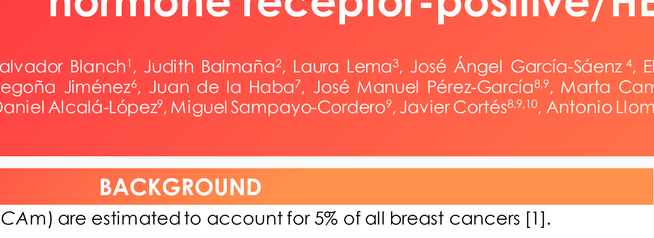
- Germline *BRCA* mutation (g*BRCA*m) are estimated to account for 5% of all breast cancers [1].
- *BRCA1* and *BRCA2* are tumor suppressor genes that encode proteins involved in the repair of DNA through the homologous recombination repair pathway [2].
- Similarly, tumors with homologous recombination deficiency (HRD) are unable to repair DNA efficiently and may derive benefit from platinum-based chemotherapy and PARP inhibitors, which have demonstrated efficacy in treating gBRCAm advanced breast cancer [3-6].
- Niraparib is a potent, highly selective, PARP 1/2 inhibitor that has demonstrated efficacy in both ovarian and breast cancer [7,8].
- The LUZERN trial aimed to evaluate the safety and efficacy of niraparib with aromatase inhibitors for pretreated HR[+]/HER2[-] advanced breast cancer with g*BRCA*m or germline *BRCA* wild-type (g*BRCA*wt) with HRD.

STUDY DESIGN

Figure 1. LUZERN Trial

Key Inclusion Criteria

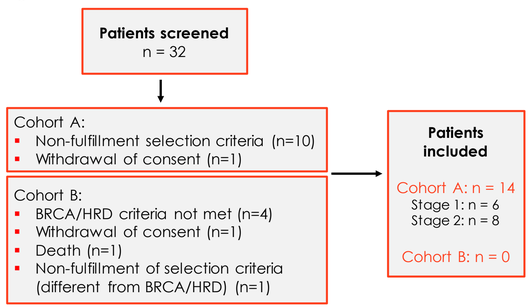
- Men/pre- and post-menopausal women with HR[+]/HER2[-] advanced breast cancer
- ≤ 1 prior regimen of chemotherapy for advanced breast cancer
- At least 1 and up to 2 prior lines of endocrine therapy for advanced breast cancer
- Confirmed progressive disease during last aromatase inhibitor-containing regimen with secondary endocrine resistance criteria
- Evaluable or measurable disease as per RECIST 1.1



CBR defined as the percentage of patients who experience a CR, PR or (SD or non-CR/non-PD for at least 24 weeks).

RESULTS

Figure 2. Patient Recruitment



1. Recruitment and Patient Disposition

- From June 15, 2020 to November 17, 2022, 14 patients were enrolled in Cohort A **(Figure 2 and Table 1)**.
- No patients were enrolled in exploratory Cohort B **(Figure 2)**.
- Data cutoff: November 14, 2023
- The median follow-up time was 16.7 months (IQR, 13.2 -18.2).

RESULTS

Table 1. Patient baseline characteristics

Baseline characteristics	n (%)
Age, Median (Min; max), years	46 (32;83)
ECOG	
0	8 (57.1%)
1	6 (42.9%)
Visceral involvement	
No	4 (28.6%)
Yes	10 (77.8%)
Number of organ sites	
1	3 (21.4%)
2	5 (35.7%)
≥ 3	6 (42.9%)
Previous treatment with targeted therapy for advanced disease	
CDK4/6 inhibitor	13 (92.9%)
mTOR inhibitor	1 (7.1%)
Previous lines of chemotherapy for advanced disease	
0	9 (64.3%)
1	5 (35.7%)
Previous lines of systematic therapy for advanced disease	
0	1 (7.1%)
1	6 (42.9%)
2	3 (21.4%)
≥3	4 (28.6%)
Patients treated with an AI different from the last AI containing regimen	
No	8 (57.1%)
Yes	6 (42.9%)

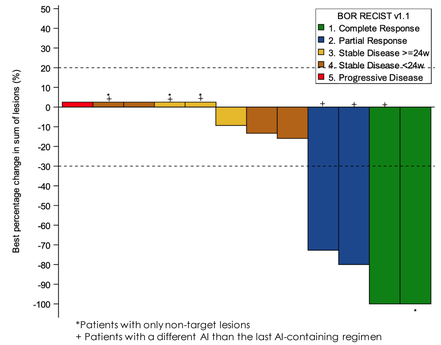
2. Efficacy Results – Cohort A

- The **CBR** in cohort A was **50.0%** (95%CI, 23.0-77.0) **(Table 2 and Figure 3)**.
- The ORR was 28.6% (95%CI, 8.4-58.1). Two patients achieved a complete response, and two patients had a partial response **(Table 2 and Figure 3)**. Median PFS was 6.9 months (95%CI, 4.9-10.5) **(Figure 4)**. Median OS was 18.1 months (95%CI, 16-NE) **(Figure 5)**.
- **Patient subgroups**
- For patients with an AI different from the last AI-containing regimen (n=6), the CBR was 83.5% (95%CI, 35.9-99.6), the ORR was 50.0% (95%CI, 11.8-88.2), and the median PFS was 9.3 months (95%CI, 4.9-11.1).
- For patients with the same AI as in the last AI-containing regimen (n=8), the CBR was 25.0% (95%CI, 3.2-65.1), the ORR was 12.5% (95%CI, 0.3-52.7), and the median PFS was 5.5 months (95%CI, 3.9-6.9).

Table 2. Cohort A efficacy endpoints

CBR, n(%)	7 (50.0%)	ORR, n(%)	4 (28.6%)
CR	2 (14.3%)	TTR, median (min; max), months	1.7 (1.7;3.9)
PR	2 (14.3%)		
SD ≥ 24w	3 (21.4%)	DoR, median (min; max), months	5.6 (3.3;8.8)
SD < 24w	4 (28.6%)		
PD	1 (7.1%)		
NE	2 (14.3%)		

Figure 3. Cohort A best percentage change of lesions



*Patients with only non-target lesions
+ Patients with a different AI than the last AI-containing regimen

Figure 4. Progression-free survival from Cohort A

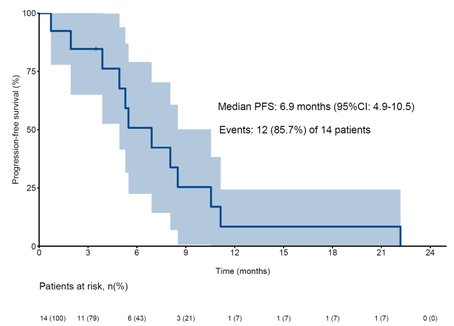
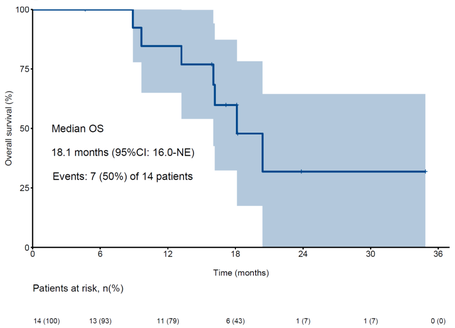


Figure 5. Overall survival from Cohort A



3. Safety Results – Cohort A

- The most common treatment-emergent adverse events (TEAEs) were fatigue (71.4%), nausea (57.1%), and neutropenia (50.0%) **(Table 3)**.
- No treatment-related G4 TEAEs nor treatment-related deaths were reported.
- Serious TEAEs occurred in 3 (21.4%) patients.
- Seven (50.0%) patients had a niraparib dose reduction and one patient experience G2 anxiety related to niraparib that lead to permanent discontinuation.

Table 3. TEAEs and Related TEAEs in >10% of patients in Cohort A

Overall (N =14) n (%)	TEAES		Related TEAEs	
	Any	G3	Any	G3
Any	13 (92.9%)	6 (42.9%)	10 (71.4%)	4 (28.6%)
Hematologic				
Neutropenia	7 (50.0%)	1 (7.1%)	5 (35.7%)	1 (7.1%)
Anemia	7 (50.0%)	2 (14.3%)	3 (21.4%)	1 (7.1%)
Thrombocytopenia	4 (28.6%)	1 (7.1%)	2 (14.3%)	1 (7.1%)
Leukopenia	2 (14.3%)	0 (0.0%)	1 (7.1%)	0 (0.0%)
Non-hematologic				
Fatigue	10 (71.4%)	0 (0.0%)	5 (35.7%)	0 (0.0%)
Nausea	8 (57.1%)	1 (7.1%)	7 (50%)	1 (7.1%)
Vomiting	4 (28.6%)	1 (7.1%)	4 (28.6%)	1 (7.1%)
Abdominal discomfort	2 (14.3%)	0 (0.0%)	1 (7.1%)	0 (0.0%)
Constipation	2 (14.3%)	0 (0.0%)	1 (7.1%)	0 (0.0%)
Limb discomfort	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Musculoskeletal chest pain	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Palpitations	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

CONCLUSIONS

- In this small study of 14 patients, niraparib in combination with aromatase inhibitors demonstrated encouraging antitumor activity and a manageable safety profile for patients with aromatase inhibitor-resistant HR[+]/HER2[-] advanced breast cancer with g*BRCA*m.
- These results warrant further investigation in larger cohorts.

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ACKNOWLEDGEMENTS

We would like to thank the patients and their families, the trial teams at the participating sites, the trial team at MEDSIR, and GSK for funding this research.

CONFLICTS OF INTEREST

Salvador Blanch, MD reports no COIs

Scan here to view a plain language summary of this trial.

Abbreviations: AI: aromatase inhibitor; CBR: clinical benefit rate; CR: complete response; DoR: duration of response; g*BRCA*m: germline *BRCA* mutation; g*BRCA*wt: germline *BRCA* wild type; HRD: homologous recombination deficiency; n: number of patients; NE: not evaluable; ORR: objective response rate; OS: overall survival; PD: progressive disease; PFS: progression-free survival; PR: partial response; SD: stable disease; TEAEs: Treatment Emergent Adverse Events; TTR: time to response; w: weeks; 95%CI: 95% Confidence Interval