Sustained long-term responders to niraparib maintenance in recurrent platinum-sensitive high-grade ovarian cancer (PSROC): a subanalysis of the GEICO-88R study

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BACKGROUND

The GEICO-88R study assessed the real-world use of niraparib as maintenance treatment in patients with PSROC (*Cueva et al, EJC 2023*), within the Spanish expanded access programme [1]. A preplanned subanalysis of long-term responders (niraparib exposure ≥12 months) was also reported (*Cueva et al, ESMO 2023, 795-P*) [2]. And, more recently, an additional subanalysis with extended follow-up was communicated in this population (*Cueva et al, ESMO GYN 2024, 55P*) [3].

OBJECTIVE

The goal of this work was to perform a post-hoc subanalysis of sustained long-term responders (SLTR); patients with niraparib exposure ≥24 months.

METHODS

In this retrospective study across 57 Spanish sites, patients received niraparib at a fixed 300 mg/day starting dose (FSD) or an individualized starting dose (ISD), 200 or 300 mg/day, according to weight and platelet count. In the current analysis a specific assessment of SLTR was performed, focusing on patient characteristics, niraparib dosing, effectiveness, tolerability, and post-niraparib systemic treatments. The results are presented in the poster comparing both the SLTR and non-SLTR (NSLTR) populations.

RESULTS

- Of 316 patients (general study), 61 (19.3%) SLTR were analyzed. In addition, NSLTR patients were also assessed.
- 82% were BRCAwt, with median of 2 prior treatment lines and relevant comorbidities *(Table 1)*.
- Median niraparib initial dose was 200 mg/day. FSD/ISD was used in 16 (26.2%) and 45 (73.8%) patients, respectively. 37.7% of patients discontinued niraparib due to progression, 3.3% toxicity and 4.9% because of physician/patient decision *(Table 2)*.
- The most frequent all-grade adverse events were thrombocytopenia, anemia and asthenia (fatigue). One acute myeloid leukemia (AML) was observed *(Figure 1)*.
- 69.2% overall response rate (ORR) was achieved in the 26 patients with assessable pre-niraparib measurable disease; vs 20.6% in 116 NSLTR. With a median follow-up of 57 months, mPFS was 47.3 months (95% CI 28.8-NA). mPFS2 and mOS were not reached *(Figures 2, 3, 4)*.
- 27 patients (44.3%) had ≥1 post-niraparib systemic treatment, in 23 patients (85.1%) was platinum-based *(Table 3)*. ORR with the first subsequent line was 33.3%. mPFS of first post-niraparib line was 7.8 months (95% CI 3.6-17.5) vs 7.4 months (95% CI 6.2-8.1) in the NSLTR group.
- Upon analysis, 31 (50.8%) patients remained on niraparib therapy, and 42 (68.9%) patients were still alive, 15 (24.6%) of them without apparent illness. 56 (91.8%) and 41 (67.2%) patients were alive at 3 and 5 years, respectively.

Figure 1. Niraparib toxicities

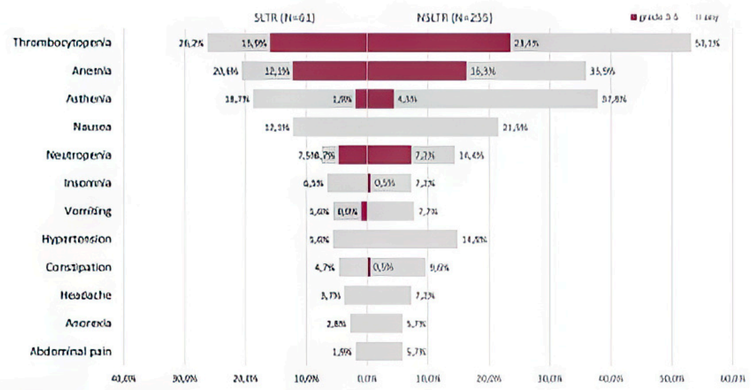


Table 1. Patient characteristics

		SLTR (N=61)	NSLTR (N=255)
Median age		61 (45-80)	64 (31-88)
Most common initial FIGO	IIIC	**36 (59.0%)***	**122 (47.8%)**
	IVA	4 (6.6%)	31 (12.2%)
	IVB	**0 (0.0%)**	**43 (16.9%)**
BRCA status	BRCAmut	4 (6.6%)	14 (5.5%)
	BRCAwt	50 (82.0%)	204 (80.0%)
	Unknown	7 (11.5%)	37 (14.5%)
Median previous chemotherapy lines		2 (1-8)	3 (1-11)
1		1 (1.6%)	5 (2.0%)
2-4		**57 (93.4%)**	**207 (81.1%)**
>4		**3 (4.9%)**	**43 (16.8%)**
Previous bevacizumab and PARPi	Bevacizumab	24 (39.3%)	118 (46.2%)
	PARPi	2 (3.3%)	21 (8.2%)
Surgery after relapse	R0	15 (71.4%)	33 (63.5%)
	R>0	4 (19.0%)	13 (25.0%)
	Unknown	2 (9.5%)	6 (11.5%)
ECOG	0	**38 (62.3%)**	**121 (47.5%)**
	1	**23 (37.7%)**	**127 (49.8%)**
	Unknown	0 (0.0%)	7 (2.7%)
Pre-niraparib measurable and assessable disease**	Yes	**26 (42.6%)**	**116 (45.5%)**
	No	**35 (57.7%)**	**139 (54.5%)**
Most common relevant comorbidities		29 (47.5%)	100 (39.2%)
Arterial hypertension		**13 (44.8%)**	**62 (62.0%)**
Diabetes mellitus		**3 (10.3%)**	**21 (21.0%)**
Obesity		4 (13.8%)	8 (8.0%)

Table 2. Treatment disposition

		SLTR (N=61)	NSLTR (N=255)
Initial dose (mg)	200	38 (62.3%)	140 (54.9%)
	300	23 (37.7%)	115 (45.1%)
Individualized	Yes (ISD)	45 (73.8%)	194 (76.1%)
	No (FSD)	16 (26.2%)	61 (23.9%)
Median dose (mg)		200	200
Treatment duration (months)	Median	57.2 (24.4-77.3)	5.6 (0.2-22.5)
	0-12	0 (0.0%)	211 (82.7%)
	12-24	0 (0.0%)	44 (17.3%)
	>24	61 (100.0%)	0 (0.0%)
Dose interruptions		46 (75.4%)	154 (60.3%)
Dose reductions		46 (75.4%)	142 (55.6%)
Still on treatment upon analysis		31 (50.8%)	0 (0.0%)
End of treatment (other than progression)	Toxicity	2 (3.3%)	15 (5.8%)
	Physician's decision	1 (1.6%)	7 (2.7%)
	Patient's decision	2 (3.3%)	4 (1.6%)
	Other	2 (3.3%)	5 (1.9%)

** Results with bold letters indicate significant (>10% difference) relevance.*
*** From patients with measurable disease before niraparib, ORR was calculated in those having assessable RECIST 1.1 response.*

Table 3. First and second lines after niraparib

PBT: Platinum-based treatment. PRS: Platinum-resistant scheme (other than paclitaxel).

	SLTR (N = 61) - N (%)	NSLTR (N = 255) - N (%)
1st line after niraparib	**27 (44.3)**	**201 (78.8)**
PBT + bevacizumab	5 (18.5)	24 (11.9)
PBT	11 (40.7)	85 (33.3)
Paclitaxel + bevacizumab	--	25 (9.8)
Paclitaxel	--	10 (3.9)
PRS + bevacizumab	--	8 (3.1)
PRS	--	11 (4.3)
PARPi	--	4 (1.5)
Other	11 (40.7)	34 (13,3)
2nd line after niraparib	**19 (31.1)**	**146 (72.6)**
PBT + bevacizumab	1 (5.2)	--
PBT	6 (31.5)	27 (18.4)
Paclitaxel + bevacizumab	2 (10.5)	17 (11.6)
Paclitaxel	2 (10.5)	25 (17.1)
PRS + bevacizumab	1 (5.2)	4 (2.7)
PRS	2 (10.5)	17 (11.6)
PARPi	1 (5.2)	5 (3.4)
Other	4 (20.8)	51 (34.9)

Figure 2. Progression-free survival (47.3 mo SLTR vs 6.2 mo non-SLTR)

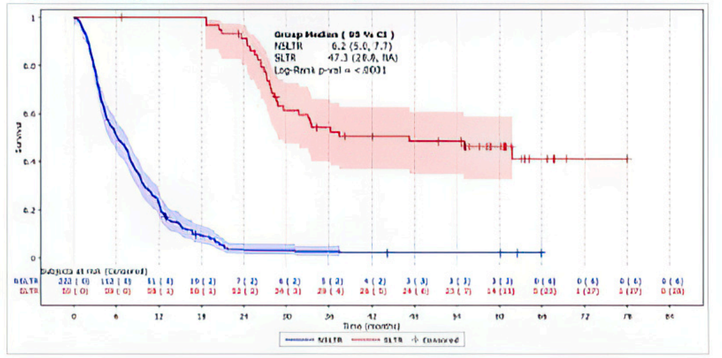


Figure 3. Progression-free survival 2 (NA SLTR vs 16.5 mo non-SLTR)

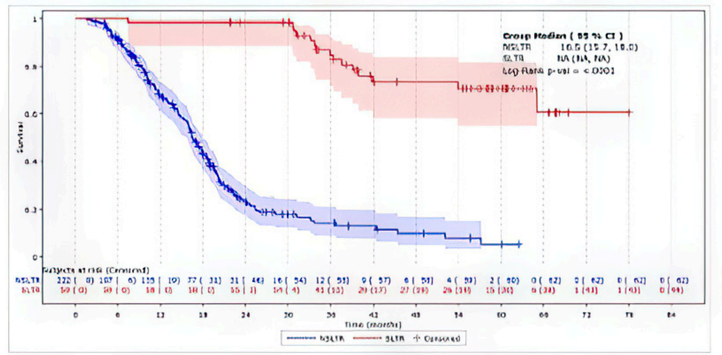
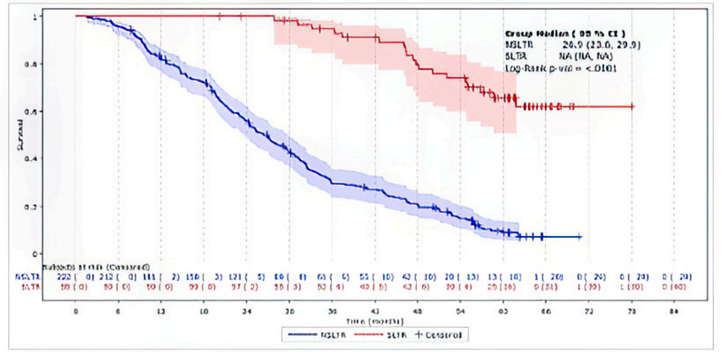


Figure 4. Overall survival (NA SLTR vs 26.9 mo non-SLTR)



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1.- Real-world safety and effectiveness of maintenance niraparib for platinum-sensitive recurrent ovarian cancer: A GEICO retrospective observational study within the Spanish expanded-access programme. European Journal of Cancer, January 2023.
2.- 795P – Tolerability and effectiveness of niraparib in long-term responders with platinum-sensitive recurrent ovarian cancer (GEICO-88R study). Poster presentation. ESMO 2023.
3.- 55P – Long-term responders (LTR) with niraparib maintenance in platinum-sensitive recurrent high-grade serous ovarian cancer (PSROC) focusing on subsequent therapies and post-progression outcomes (GEICO-88R study). Poster presentation. ESMO GYN 2024.

CONCLUSIONS

This subanalysis of SLTR to niraparib maintenance in real life shows a significant proportion of patients (nearly 20% of the total) with remarkable benefit (≥24 months), some of them without detectable tumour. Two thirds of patients are alive at 5 years and mOS is not reached despite being a high-risk population. Most of them received a platinum-based treatment as next systemic line after niraparib progression. Although it is impossible to identify significant predictors from a retrospective descriptive study, in addition to better tolerability and niraparib responses, there are relevant differences between the SLTR and NSLTR populations (highlighted in bold) that could explain the divergent outcomes.

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