

HEALTH RELATED QUALITY OF LIFE (HRQOL) REVIEW IN PATIENTS WITH OVARIAN CANCER: A SYSTEMATIC LITERATURE REVIEW (SLR)

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BACKGROUND

- Ovarian cancer (OC) ranks fifth in cancer deaths among women, accounting for more deaths than any other gynecological cancer in the United States¹.
- Use of maintenance poly (ADP-ribose) polymerase inhibitors (PARPi) in platinum-sensitive recurrent epithelial ovarian cancer has significantly improved PFS and reduced time on chemotherapy². PARPi are generally well-tolerated with any toxicities (nausea, fatigue, myelosuppression) being considered manageable.
- ESMO and NCCN guidelines state that PARPi may be used for maintenance therapy irrespective of BRCA status following a response to platinum-based therapy in patients with recurrent platinum-sensitive high-grade ovarian cancer^{3,4}.
- Few published studies have yet to examine HRQoL estimates associated with PARPi use despite being essential components of an effectiveness analysis for these treatments.
- This study reviewed published literature on HRQoL measures used in trials involving ovarian cancer patients treated with a PARPi as maintenance in 1L or greater following platinum-based therapy.

METHODS

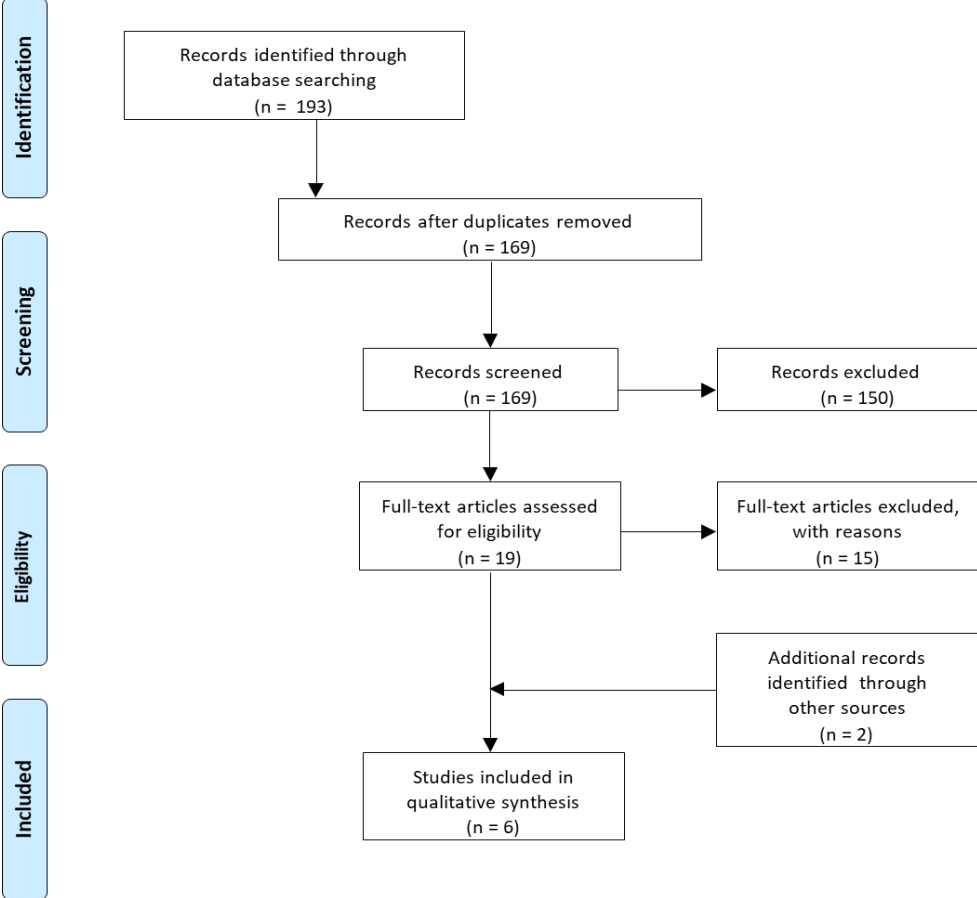
Literature Review Methodology

- A SLR was conducted using the Population, Intervention, Comparator, Outcome, Study Design (PICOS) model.
- Cochrane Library, Medline via Embase, and PubMed were searched for articles in English (January 2012-July 2020) that addressed HRQoL measured by patient reported outcomes in recurrent epithelial ovarian, fallopian tube and primary peritoneal cancers in treatment with PARPi.
- PARPi therapies of note included: olaparib, rucaparib, and niraparib

Table 1. HRQoL Literature Review PICOS

PICOS	Inclusion Criteria	Exclusion Criteria
Population	• Adult patients (≥ 18 years) with OC	• Children
Interventions and Comparators	• Platinum sensitive 1st line maintenance therapy either recommended or prescribed for management of OC	• Phase 1 Trial
Outcomes	• Studies utilizing questionnaires containing HRQoL outcomes	• None to limited reported values
Study Designs	• Observational studies • Comparative studies • Non-comparative studies • PRO studies	• N/A

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram with the identified HRQoL studies



*Key databases included Cochrane (n=39), PubMed (n=70), and Embase (n=84).

RESULTS

- Six studies met the final criteria for inclusion with three PARPi (olaparib, niraparib, and rucaparib) identified to have HRQoL data.
- There was no single tool or result common across all assessed interventions. Instruments used in these assessments included:
 - EuroQoL five-dimension scale (EQ-5D)
 - Functional Assessment of Cancer Therapy-Ovarian Cancer symptom index (FOSI)
 - Trial Outcomes Index (TOI)
 - Quality-Adjusted Progression-Free Survival (QAPFS)
 - Functional Assessment of Cancer Therapy-Ovarian (FACT-O)
- Niraparib was comparable to placebo when measured via EQ-5D and FOSI in 2 studies
- Olaparib was comparable to placebo via FOSI, FACT-O, and TOI where a clinically meaningful difference was defined as ±10% in TOI⁸.
- Both olaparib and rucaparib had longer QAPFS than placebo.
- There was limited data differentiating HRQoL outcomes among BRCA sub-populations (i.e. germline, somatic or wild-type).

Table 2. HRQoL assessment measures point estimates for niraparib, olaparib, and rucaparib as maintenance treatments compared to placebo

PARPi	HRQoL Tool	Author	Maintenance Therapy	Outcomes	Germline BRCA Cohort Treatment	Germline BRCA Cohort Placebo	Non-germline BRCA Cohort Treatment	Non-germline BRCA Cohort Placebo	Overall Treatment	Overall Placebo
Niraparib	EQ-5D	Mirza 2016 ^{*5}	2L+	Baseline	0.851	0.849	0.839	0.836	N/R	N/R
				Post-Progression	0.816	0.832	0.800	0.780	N/R	N/R
	EQ-5D	Oza 2018 ^{*6}	2L+	Baseline	0.850	0.847	0.837	0.824	N/R	N/R
				Post-Progression	0.801	0.794	0.810	0.783	N/R	N/R
FOSI	Mirza 2016 ^{*5}	2L+	2L+	Baseline	24.8	24.9	25.0	24.9	N/R	N/R
				Post-Progression	23.8	23.7	22.5	22.9	N/R	N/R
FOSI	Oza 2018 ^{*6}	2L+	2L+	Baseline	25.1	25.6	25.4	25.0	N/R	N/R
				Post-Progression	N/R	N/R	N/R	N/R	N/R	N/R
Olaparib	FOSI	Ledermann 2016 ⁷	2L+	Baseline (SD)	25.8 (3.3)	25.1 (4.1)	25.9 (3.4)	24.8 (4.1)	26.1 (3.4)	25.4 (3.8)
				% Reporting Improved [#]	26.1%	12.8%	21.2%	16.1%	17.1%	14.8%
	FACT-O	Ledermann 2016 ⁷	2L+	Baseline (SD)	119.5 (18.5)	118.6 (17.2)	118.9 (18.1)	115.9 (18.9)	121.9 (17.3)	119.7 (17.4)
				% Reporting Improved [#]	28.9%	10.8%	27.0%	20.8%	21.1%	18.9%
	TOI	Ledermann 2016 ⁷	2L+	Baseline (SD)	79.5 (12.3)	81.0 (11.0)	79.9 (12.1)	79.5 (12.1)	81.7 (11.8)	81.5 (11.6)
				% Reporting Improved [#]	26.7%	8.1%	25.0%	18.9%	20.0%	18.0%
	TOI	Moore 2018 ⁸	1L	Baseline	N/R	N/R	N/R	N/R	73.6	75.0
				AAMC after 2 years (95% CI)	N/R	N/R	N/R	N/R	0.30	3.30
				Group Difference (95% CI)		N/R		N/R	(-0.72 to 1.32)	(1.84 to 4.76)
	TOI	Friedlander 2018 ^{9**}	2L+	Baseline (SD)	N/R	N/R	N/R	N/R	75.26 (13.78)	77.12 (11.35)
				AAMC post progression (95% CI)	N/R	N/R	N/R	N/R	-2.90	-2.87
				Group Difference (95% CI)		N/R		N/R	(-4.13 to -1.67)	(-4.64 to -1.10)
QAPFS	Friedlander 2018 ^{9**}	2L+	2L+	Overall Months (SD)	N/R	N/R	N/R	N/R	13.96 (10.96)	7.28 (5.22)
				Overall Months (95% CI)	N/R	N/R	N/R	N/R	15.28 (13.22 to 17.45)	5.92 (4.71 to 7.23)
				Mean Difference (95%CI)		N/R		N/R	9.37 Months (6.65 to 11.85)	
Rucaparib	QAPFS	Oza 2020 ^{***10}	2L+	Overall Months (95% CI)	N/R	N/R	N/R	N/R	15.28 (13.22 to 17.45)	5.92 (4.71 to 7.23)

*ENGOT-OV16/NOVA; **SOLO2/ENGOT Ov-21; ***ARIEL3; [#]% of people who had best response as “improved”; NR = Not Reported; AAMC = Adjusted Average Mean Change

CONCLUSIONS

- The advent of PARPi has improved the outcomes of patients with recurrent OC. Side-effects of PARPi (e.g. nausea, fatigue and myelosuppression) are usually well-managed.
- However, other than QAPFS, most of the HRQoL measures do not seem to capture the improved manageability of side effects when patients are treated with PARPi. PRO data do not follow a similar pattern as the other efficacy outcomes (i.e. no differences were found in HRQoL between control and treatment groups in reviewed studies).
- This could be that current validated PRO instruments may not be fully fit-for-purpose to measure the effects of targeted therapies as the existing instruments were developed when chemotherapy was the standard of care. Additionally, more information is needed on the long-term HRQoL effects of PARPi in the maintenance setting.
- Further HRQoL research especially related to PARPi use in long-term maintenance, both in clinical trials and the real-world, is needed while development of new fit-for-purpose PROs should be considered.

REFERENCES

1. American Cancer Society. Cancer Facts & Figures 2021. Atlanta, Ga: American Cancer Society; 2021. April 27, 2021.
2. Cook SA, Tinker AV. PARP Inhibitors and the Evolving Landscape of Ovarian Cancer Management: A Review. BioDrugs. 2019 Jun;33(3):255-273. doi: 10.1007/s40259-019-00347-4.
3. National Comprehensive Cancer Network. Ovarian Cancer. <https://www.nccn.org/patients/guidelines/content/PDF/ovarian-patient.pdf>. Accessed March 15, 2021.
4. ESMO Guidelines Committee. eUpdate -1 April 2020. ESMO. <https://www.esmo.org/guidelines/gynaecological-cancers/newly-diagnosed-and-relapsed-epithelial-ovarian-carcinoma/eupdate-ovarian-cancer-treatment-recommendations>. Accessed March 15, 2021.
5. Mirza MR, Monk BJ, Herrstedt J, Oza AM, Mahner S, Redondo A, Fabbro M, Ledermann JA, Lorusso D, Vergote I, Ben-Baruch NE. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. New England Journal of Medicine. 2016 Dec 1;375(22):2154-64.
6. Oza AM, Matulonis UA, Malander S, Hudgens S, Sehoul J, Del Campo JM, Berton-Rigaud D, Banerjee S, Scambia G, Berek JS, Lund B. Quality of life in patients with recurrent ovarian cancer treated with niraparib versus placebo (ENGOT-OV16/NOVA): results from a double-blind, phase 3, randomised controlled trial. The Lancet Oncology. 2018 Aug 1;19(8):1117-25.
7. Ledermann JA, Harter P, Gourley C, Friedlander M, Vergote I, Rustin G, Scott C, Meier W, Shapira-Frommer R, Safra T, Matei D. Quality of life during olaparib maintenance therapy in platinum-sensitive relapsed serous ovarian cancer. British journal of cancer. 2016 Nov;115(11):1313-20.
8. Moore K, Colombo N, Scambia G, Kim BG, Oaknin A, Friedlander M, Lisysanskaya A, Floquet A, Leary A, Sonke GS, Gourley C, Banerjee S, Oza A, González-Martin A, Aghajanian C, Bradley W, Mathews C, Liu J, Lowe ES, Bloomfield R, DiSilvestro P. Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med. 2018 Dec 27;379(26):2495-2505. doi: 10.1056/NEJMoa1810858. Epub 2018 Oct 21. PMID: 30345884.
9. Friedlander M, Gelski V, Gibbs E, Davies L, Bloomfield R, Hilpert F, Wenzel LB, Eek D, Rodrigues M, Clamp A, Penson RT. Health-related quality of life and patient-centred outcomes with olaparib maintenance after chemotherapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT Ov-21): a placebo-controlled, phase 3 randomised trial. The Lancet Oncology. 2018 Aug 1;19(8):1126-34.
10. Oza AM, Lorusso D, Aghajanian C, Oaknin A, Dean A, Colombo N, Weberpals JL, Clamp AR, Scambia G, Leary A, Holloway RW. Patient-centered outcomes in ARIEL3, a phase III, randomized, placebo-controlled trial of Rucaparib maintenance treatment in patients with recurrent ovarian carcinoma. Journal of Clinical Oncology. 2020 Oct 20;38(30):3494.

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