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 States[1].
- Use of maintenance poly (ADP-ribose) polymerase inhibitors (PARP*i*) in platinum-sensitive recurrent epithelial ovarian cancer has significantly improved PFS and reduced time on chemotherapy[2]. PARP*i* are generally well-tolerated with any toxicities (nausea, fatigue, myelosuppression) being considered manageable.
- ESMO and NCCN guidelines state that PARP*i* 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 PARP*i* 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 PARP*i* as maintenance in 1L or greater following platinum-based therapy.

METHODS

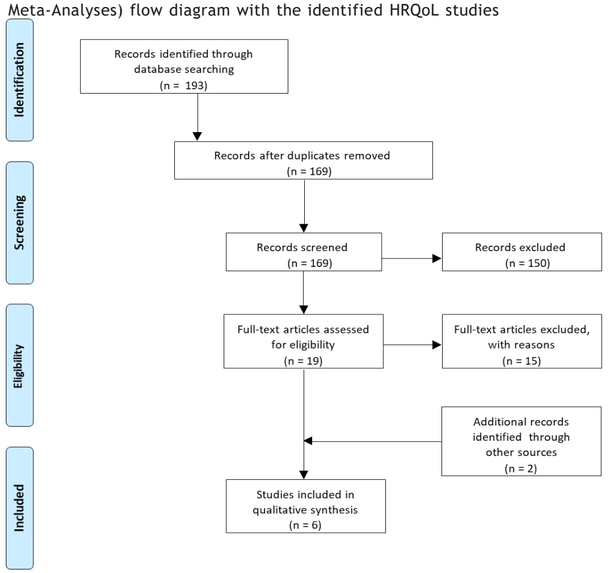
Literature Review Methodology

- 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 PARP*i*.
- PARP*i* 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 PARP*i* (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 TOI[8].
- 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

PARP*i*	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+	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+	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 (-0.72 to 1.32)	3.30 (1.84 to 4.76)
				Group Difference (95% CI)	N/R		N/R		-3.00 (-4.78 to -1.22)	
	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 (-4.13 to -1.67)	-2.87 (-4.64 to -1.10)
				Group Difference (95% CI)	N/R		N/R		-0.03 (-2.19 to 2.13)	
	QAPFS	Friedlander 2018**[9]	2L+	Overall Months (SD)	N/R	N/R	N/R	N/R	13.96 (10.96)	7.28 (5.22)
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)
				Mean Difference (95%CI)	N/R		N/R		9.37 Months (6.65 to 11.85)	

*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 PARP*i* has improved the outcomes of patients with recurrent OC. Side-effects of PARP*i* (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 PARP*i*. 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 PARP*i* in the maintenance setting.
- Further HRQoL research especially related to PARP*i* 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.

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