

SUPPLEMENTARY APPENDIX

Genetic counseling, testing and management of of of epithelial ovarian carcinoma

Table 1. Systematic evaluation of the selected CPGs, with the AGREE II instrument ⁽¹⁾.

Name of the Guide	Reach and Objectives (%) ^a	Participation of those involved (%) ^b	Rigor in the elaboration (%) ^c	Clarity of presentation (%) ^d	Applicability (%) ^e	Editorial independence (%) ^f	Global Assessment
National Comprehensive Cancer Network (NCCN) Breast and/or Ovarian Cancer Genetic Screening Guidelines V2 2021 ⁽²⁾ .	100%	89%	95%	100%	81%	100%	100%
NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ .	97%	92%	94%	94%	71%	100%	100%
National Institute for Clinical Excellence (NICE) clinical guideline on familial breast cancer, 2013 ⁽⁴⁾ .	97%	94%	96%	92%	77%	100%	83%
Scottish Intercollegiate Ovarian Epithelial Cancer Management Guidelines. Guidelines Network (SIGN) 135", 2018 ⁽⁵⁾ .	89%	97%	94%	89%	88%	96%	83%
American Society of Clinical Oncology (ASCO) Guidelines for Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer, 2020 ⁽⁶⁾ .	100%	94%	85%	97%	63%	100%	83%
Guidelines for the treatment of ovarian cancer including primary peritoneal and fallopian tube cancer from the "Japan Society of Gynecologic Oncology (JSGO)", 2020 ⁽⁷⁾ .	100%	97%	91%	92%	42%	100%	83%
ASCO PARP Inhibitor Ovarian Cancer Management Guidelines, 2020 ⁽⁸⁾ .	92%	92%	80%	89%	67%	100%	83%
French Society of Predictive and Personalized Medicine (SFMPP) Clinical Practice Guidelines for <i>BRCA1</i> and <i>BRCA2</i> , 2021 ⁽⁹⁾ .	100%	92%	69%	92%	13%	100%	83%
Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer "European Society of Medical Oncology ESMO", 2020 ⁽¹⁰⁾ .	83%	44%	88%	100%	17%	100%	83%
Society of Obstetricians and Gynecologists of Canada (SOGC) guideline for the gynecologic management of Hereditary ovarian cancer, 2018 ⁽¹¹⁾ .	94%	67%	81%	89%	10%	67%	75%
Clinical practice guidelines for prevention and screening in carriers of BRCA mutations and other hereditary breast/ovarian syndromes from the "European Society for Medical Oncology (ESMO)", 2016 ⁽¹²⁾ .	75%	44%	66%	86%	15%	83%	75%
Consensus guidelines for genetic counseling, testing, and management of hereditary breast and ovarian cancer (HBOC) from the Indian Society of Medical and Pediatric Oncology, 2020 ⁽¹³⁾ .	83%	53%	49%	94%	29%	83%	67%
Clinical guidelines on hereditary breast and ovarian cancer of the "Sociedad Española de Oncología Médica (SEOM)", 2019 ⁽¹⁴⁾ .	75%	39%	17%	86%	21%	88%	50%
American College of Medical Genetics and Genomics (ACMG) Cancer Predisposition Screening Referral Indications Guideline, 2015 ⁽¹⁵⁾ .	56%	47%	34%	78%	13%	71%	50%

^aDegree to which the overall objectives of the guideline and the clinical questions were covered. ^bDegree to which the guidelines represent the opinions of the final recipients. ^cDegree to which systematic methods were taken into account in formulating the recommendations. ^dClarity of the guidelines and whether the recommendations are specific and unambiguous. ^eEvaluation of the problems of implementing the guidelines. ^fEditorial independence.

Table 2. Rating of the quality of evidence according to GRADE ⁽¹⁶⁾.

High	High confidence that the effect estimator available in the scientific literature is very close to the real effect.
Moderate	The effect estimator is likely to be close to the actual effect, although there could be substantial differences.
Low	The effect estimator may be substantially different from the actual effect.
Very Low	It is very likely that the effect estimator will be substantially different from the actual effect.

Table 3. Strength and direction of recommendation according to GRADE ⁽¹⁶⁾.

Strong recommendation in favor	The benefits of the intervention clearly outweigh the undesirable effects.
Conditional (or weak) recommendation in favor	The benefits of the intervention probably outweigh the undesirable effects.
Conditional (or weak) recommendation against	The undesirable effects of the intervention probably outweigh the benefits.
Strong recommendation against	The undesirable effects of the intervention clearly outweigh the benefits.

Table 4. Genes to be evaluated in patients with epithelial ovarian cancer.

Gen to be evaluated	Definition	Increased risk of cancer (type of evidence)^a
<i>BRCA1</i>	Breast cancer susceptibility gene 1	Very strong evidence of increased risk ⁽¹⁷⁾ .
<i>BRCA2</i>	Breast cancer susceptibility gene 2	Very strong evidence of increased risk ⁽¹⁷⁾ .
<i>ATM</i>	Ataxia telangiectasia mutated	Strong evidence of increased risk ^(18–20) .
<i>BRIP1</i>	BRCA1 Interacting Helicase 1	Strong evidence of increased risk ^(18–20) .
<i>MLH1</i>	MutL homolog 1	Strong evidence of increased risk ^(21,22) .
<i>MSH2</i>	MutS homolog 2	Strong evidence of increased risk ^(21,22) .
<i>MSH6</i>	MutS homolog 6	Strong evidence of increased risk ^(21,22) .
<i>PALB2</i>	Partner and localizer of BRCA2	Strong evidence of increased risk ^(18–20,23) .
<i>RAD51C</i>	RAD51 paralog C	Strong evidence of increased risk ^(18–20,24) .
<i>RAD51D</i>	RAD51 paralog D	Strong evidence of increased risk ^(18–20,24) .
<i>TP53</i>	Tumor protein p53	Strong evidence of increased risk ^(20,25,26) .
<i>PTEN</i>	Phosphatase And Tensin Homolog	Strong evidence of increased risk ^(20,25,26) .
<i>PMS2</i>	Post-meiotic segregation increased 2	Limited evidence of increased risk ^(27–29) .
<i>EPCAM</i>	Epithelial cellular adhesion molecule	Limited evidence of increased risk ⁽²⁷⁾ .
<i>NBN</i>	Nibrin	Limited evidence of increased risk ^(18–20) .

^aEvidence rating for increased risk (NCCN): **Very strong**, Prospective cohort studies in a population-based setting have demonstrated risk; **Strong**: Traditional case-control studies or more than 3 case-control studies including those with commercial laboratory-proven cases or those without controls from the same population. Traditional case-control study: A retrospective study comparing patients with a specific disease or outcome (cases) to patients without the disease or outcome (controls); **Limited**, small sample size or a case series None.



Table 5. Medications for maintenance treatment after first-line epithelial ovarian cancer.

Stage	BRCA 1/2	Systemic Therapy	Response to therapy on first line	Recommendation	Clinical Practice Guidelines that support the indication
I – II	Any	Platinum-based chemotherapy	Complete response/ partial response	Watch and wait	National Comprehensive Cancer Network Ovarian Cancer Guidelines NCCN V1.2021 ⁽³⁾ . NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . American Society of Clinical Oncology (ASCO) Guidelines for Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer, 2020 ⁽⁶⁾ . ASCO PARP Inhibitor Ovarian Cancer Management Guidelines, 2020 ⁽⁸⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer "European Society of Medical Oncology ESMO", 2020 ⁽¹⁰⁾ . Consensus guidelines for genetic counseling, testing, and management of hereditary breast and ovarian cancer (HBOC) from the Indian Society of Medical and Pediatric Oncology, 2020 ⁽¹³⁾ . Clinical guidelines on hereditary breast and ovarian cancer of the "Sociedad Española de Oncología Médica (SEOM)", 2019 ⁽¹⁴⁾ . Guidelines for the treatment of ovarian cancer including primary peritoneal and fallopian tube cancer from the "Japan Society of Gynecologic Oncology (JSGO)," 2020 ⁽⁷⁾ . French Society of Predictive and Personalized Medicine (SFMP) Clinical Practice Guidelines for BRCA1 and BRCA2, 2021 ⁽⁹⁾ . NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ .
				Olaparib	ASCO "Guidelines for Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer", 2020 ⁽⁶⁾ . ASCO PARP Inhibitor Ovarian Cancer Management Guidelines, 2020 ⁽⁸⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ . SFMP clinical practice guidelines for BRCA1 and BRCA2, 2021 ⁽⁹⁾ .
				Niraparib ^a	ASCO PARP Inhibitor Ovarian Cancer Management Guidelines, 2020 ⁽⁸⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ . SFMP clinical practice guidelines for BRCA1 and BRCA2, 2021 ⁽⁹⁾ .
				Therapy for persistent/recurrent disease	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ .
III – IV	Positive	Platinum-based chemotherapy + bevacizumab	Complete response/ partial response	Olaparib	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO 2020 Guidelines for Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer ⁽⁶⁾ . SFMP Clinical Practice Guidelines for BRCA1 and BRCA2, 2021 ⁽⁹⁾ .
				Olaparib + Bevacizumab	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO 2020 Guidelines for Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer ⁽⁶⁾ . ASCO PARP inhibitor ovarian cancer management guideline, 2020 ⁽⁸⁾ . SFMP Clinical Practice Guideline for BRCA1 and BRCA2, 2021 ⁽⁹⁾ .
				Niraparib ^a	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO 2020 Guidelines for Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer ⁽⁶⁾ . SFMP Clinical Practice Guideline for BRCA1 and BRCA2, 2021 ⁽⁹⁾ .
				Watch and wait	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ .
				Niraparib ^a	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO PARP inhibitor ovarian cancer management guideline, 2020 ⁽⁸⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ . SFMP Clinical Practice Guideline for BRCA1 and BRCA2, 2021 ⁽⁹⁾ .
				Therapy for persistent/recurrent disease/ bevacizumab	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ .
III – IV	Negative or Unknown	Platinum-based chemotherapy + Bevacizumab	Complete response/ partial response	Olaparib + bevacizumab (only if there is genomic instability)	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ .
				Niraparib ^a	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ .
				Therapy for persistent/recurrent disease/ bevacizumab	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ .

Table 6. Medications for maintenance treatment in recurrence of epithelial ovarian cancer.

<i>BRCA</i>	Systemic Therapy	Response to first line treatment	Recommendation	Clinical Practice Guidelines that support the indication
Positive, negative or Unknown	Platinum- based Chemotherapy	Complete response/ partial response	Olaparib	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO "Guidelines for Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer", 2020 ⁽⁶⁾ . ASCO PARP Inhibitor Ovarian Cancer Management Guidelines, 2020 ⁽⁸⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ . Consensus guideline for genetic counseling, testing, and management of HBOC from the Indian Society of Medical and Pediatric Oncology, 2020 ⁽¹³⁾ . SFMP clinical practice guideline for BRCA1 and BRCA2, 2021 ⁽⁹⁾ .
			Niraparib ^a	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO "Guidelines for Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer", 2020 ⁽⁶⁾ . ASCO PARP inhibitor ovarian cancer management guidelines, 2020 ⁽⁸⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ . Consensus guidelines for genetic counseling, testing, and management of HBOC from the Indian Society of Medical and Pediatric Oncology, 2020 ⁽¹³⁾ .
			rucaparib ^b	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO's Guide to Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer, 2020 ⁽⁶⁾ . ASCO PARP inhibitor ovarian cancer management guidelines, 2020 ⁽⁸⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ . Consensus guidelines for genetic counseling, testing, and management of HBOC from the Indian Society of Medical and Pediatric Oncology, 2020 ⁽¹³⁾ , SFMP clinical practice guidelines for BRCA1 and BRCA2, 2021 ⁽⁹⁾ ,

Table 7. Medications for treatment in recurrence of epithelial ovarian cancer.

BRCA	Systemic Therapy	Recommendation	Clinical Practice Guidelines that support the indication
Positive	Equal to or more than two lines of chemotherapy treatment	Rucaparib ^b	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO's Guide to Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer, 2020 ⁽⁶⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ . Consensus guidelines for genetic counseling, testing, and management of HBOC from the Indian Society of Medical and Pediatric Oncology, 2020 ⁽¹³⁾ . Clinical guidelines on hereditary breast and ovarian cancer of the "Sociedad Española de Oncología Médica (SEOM)", 2019 ⁽¹⁴⁾ . SFMPP clinical practice guidelines for BRCA1 and BRCA2, 2021 ⁽⁹⁾ .
	Equal to or more than three lines of chemotherapy treatment	Olaparib	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO's Guide to Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer, 2020 ⁽⁶⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ . Consensus guidelines for genetic counseling, testing, and management of HBOC from the Indian Society of Medical and Pediatric Oncology, 2020 ⁽¹³⁾ .
Positive, negative or Unknown	Equal to or more than three lines of chemotherapy treatment and who have progressed more than 6 months after response to last platinum-based chemotherapy	Niraparib ^a	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO's Guide to Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer, 2020 ⁽⁶⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ .
		Niraparib ^a (only if there is genomic instability)	NCCN Ovarian Cancer Guidelines V1.2021 ⁽³⁾ . ASCO's Guide to Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer, 2020 ⁽⁶⁾ . Recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer from ESMO, 2020 ⁽¹⁰⁾ .

^a Niraparib has not been authorized for its use in patients with ovarian cancer in Peru.

^b Rucaparib has not been authorized for its use in patients with ovarian cancer in Peru.

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