Improving Interprofessional Management and Clinical Outcomes with PARP Inhibitors for Advanced Ovarian Cancer

A PATIENT/CLINICIAN SHARED DECISION-MAKING GUIDE

What is Shared Decision-Making?

Shared decision-making (SDM) occurs when a healthcare provider and a patient work together to make a healthcare decision that is best for the patient. Optimal decision-making takes into account evidence-based information about available options; the provider's knowledge and experience; and the patient's values, goals, and preferences. Patients and their families/caregivers who are engaged in an SDM process are more likely to arrive at a treatment decision that works best for all those involved.

SHARE Decision Making Model

SEEK	your patient's participation.
HELP	your patient explore & compare treatement options.
ASSESS	your patient's values and preferences.
REACH	a decision with your patient.
EVALUATE	your patient's decision.

Identification of Patients Who Might Benefit From PARP Inhibitor Therapy

- Homologous recombination deficiency (HRD) is present in ~50% of newly-diagnosed, high-grade, epithelial ovarian cancers
  - Approximately 20% of patients with ovarian cancer harbor a BRCA mutation
  - Homologous recombination repair (HRR) gene mutations, altered gene expression, and other causes contribute to genomic instability
- PARP inhibitors trap PARP enzymes on DNA, causing cancer-specific cell death in tumors with HRD
- In the first-line maintenance setting, HRD genomic instability predicts the magnitude of PARP inhibitor benefit

Guideline Recommendations: Tumor Molecular Analyses

- Patients with ovarian cancer should have genetic risk evaluation and germline and somatic testing
- Germline and somatic BRCA1/2 status informs maintenance therapy
- In the absence of a BRCA1/2 mutation, HRD status may provide information on the magnitude of benefit of PARP inhibitor therapy

Setting	Recommendation
Upfront	Choice of somatic testing should, at a minimum, optimize identification of molecular alterations that can inform use of interventions that have demonstrated benefit in this setting, including: **BRCA1/2, LOH, or HRD status in the absence of a germline BRCA mutation**

Selecting Appropriate Patients for PARP Inhibitor Therapy and Setting Expectations Are Key

- Complete or partial response to platinum-based chemotherapy
- Able to tolerate oral medication
- No significant hepatic or renal dysfunction
- PARP inhibitor related adverse events are of low grade and manageable
- Prompt management of adverse events, especially non-hematologic issues will help with patient compliance
- Judicious use of dose interruptions over the course of therapy may help avoid dose reductions and maintain dose intensity and efficacy
- Shared decision-making: Aligning treatment planning decisions with patient centric concerns, goals, preferences, values, ethnical background, and impact on improving patient outcomes and quality of life

FDA-Approved PARP Inhibitor Maintenance for Newly-Diagnosed Advanced Ovarian Cancer

	Olaparib	Olaparib + bevacizumab	Niraparib
Approval	Maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy	Maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with HRD-positive status defined by either: • a deleterious or suspected deleterious BRCA mutation, and/or • genomic instability	Maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy
Biomarker Testing for Patient Selection	BRCA1m, BRCA2m	HRD+ (BRCA1m, BRCA2m, and/or genomic instability)	Appropriate for all patients regardless of BRCAm status
Dosing/ Administration	300mg taken orally twice daily with or without food	300mg taken orally twice daily with or without food Bevacizumab: 15 mg/kg IV every three weeks	Depending on patient weight and platelet count, 200mg or 300mg taken orally once daily with or without food
Trial	SOLO-1	PAOLA-1	PRIMA
Key Efficacy Data: Median PFS	In BRCAm: NR vs 13.8 months placebo (HR .30)	In HRD+: 37.2 months vs 17.7 months placebo + bevacizumab (HR .33)	In overall population: 13.8 months vs 8.2 months placebo (HR 0.62)
Warnings/ Precautions	MDS/AML Pneumonitis VTE Embryo-fetal toxicity	Pneumonitis VTE Embryo-fetal toxicity	MDS/AML Bone Marrow Suppression Hypertension and cardiovascular effects PRES Embryo-fetal toxicity
Monitoring	Hematologic toxicity/CBC for cytopenia New or worsening respiratory symptoms Signs/symptoms of VTE and PE		CBC Blood pressure Heart rate Signs/symptoms of PRES

AML, acute myeloid leukemia; HR, hazard ratio; HRD, homologous recombination deficiency; IV, intravenous; MDS, myelodysplastic syndrome; NR, not reached; PE, pulmonary embolism; PRES, posterior reversible encephalopathy syndrome; UTI, urinary tract infection; VTE, venous thromboembolism.

Optimal First-Line Maintenance Therapy Decisions Need to Consider Multiple Factors

Disease characteristics	• Clinical characteristics (symptoms, residual tumor) • Molecular characteristics (biomarker status)	
Drug properties	• Safety and efficacy • Ease of administration	• Individual dosing • Drug interactions
Accessibility	• Genetic *BRCA* and HRD testing • Approvals and indications	• Reimbursement • Cost
Patient characteristics	• Overall treatment plan • Comorbidities • Patient preference	• Quality of life/patient-reported outcomes

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