An Update on Ovarian Cancer with a Focus on PARP Inhibitors

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Disclosure

- I have no professional/financial disclosures regarding this presentation.

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Objectives

- Review the pathophysiology of ovarian cancer
- Summarize current treatment recommendations for ovarian cancer
- Explore new treatment options for recurrent ovarian cancer, with a focus on PARP inhibitors
- Discuss future directions for treatment of ovarian cancer

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Ovarian Cancer

Background
Anatomy/Pathophysiology
Staging
Treatment Overview

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Epidemiology

- 22,440 estimated new cases in 2017
- 14,080 estimated deaths in 2017
- Median age at diagnosis 63 y/o
- Highest prevalence in Caucasian females

Stage	Cases by Stage	5-year Relative Survival
Localized	15%	92.5%
Regional	20%	73%
Distant	60%	28.9%
Unknown	6%	25.1%

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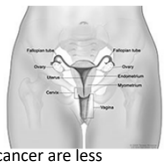
National Cancer Institute: SEER Program. https://seer.cancer.gov/statfacts/html/ovary.html

Anatomy/Pathophysiology

- Most commonly epithelial ovarian cancer (EOC)
  - High-grade serous carcinoma
- Less common histologic subtypes
  - Endometrioid/low-grade serous carcinomas
  - Clear cell carcinomas
  - Mucinous carcinomas
  - Carcinosarcoma
  - Malignant sex cord-stromal tumors
  - Malignant germ cell tumors
- Fallopian tube cancer and primary peritoneal cancer are less common but present in a similar fashion
- Common sites of metastases: liver, lung, peritoneum



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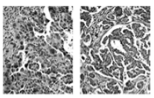
The MD Anderson Manual of Medical Oncology, 3e. New York, NY: McGraw-Hill.
National Cancer Institute: SEER Program. https://seer.cancer.gov/statfacts/html/ovary.html
National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Ovarian Cancer; v2.2017.

Histologic Subtypes



- **High-grade serous carcinomas: 70-80% of all ovarian cancers**
  - Molecular features: p53 mutation, **BRCA1 dysfunction**, PIK3CAb amplification (25%-40%)
  - Includes transitional cell carcinoma and undifferentiated carcinoma
- Low-grade serous carcinoma: 5-8% of all ovarian cancers (6%-10% of serous)
  - Molecular features: mutations in K-RAS (20-40%) and/or BRAF (5%)
- Endometrioid adenocarcinoma (high or low grade): 10% of all ovarian tumors
  - Molecular features: mutations in p53, PIK3CA, CTNNB1, PTEN; **BRCA1 dysfunction**
- Clear Cell Carcinoma: 5-10% of all ovarian cancers
  - Molecular features: PTEN mutation/loss of heterozygosity, PIK3CA mutation
- Mucinous: 3% of all ovarian cancers
  - Molecular features: mutations in K-RAS, p53

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The MD Anderson Manual of Medical Oncology, 3e. New York, NY: McGraw-Hill.

Staging

Criteria	Classification	Definition
Primary Tumor (T)	TX	Primary tumor cannot be assessed
	T0	No evidence of primary tumor
	T1	**Tumor limited to ovaries (one or both)**
	T1a	1 ovary w/ intact capsule, no tumor on ovarian surface or malignant cells in ascites/peritoneal washings
	T1b	2 ovaries w/ intact capsule, no tumor on ovarian surface or malignant cells in ascites/peritoneal washings
	T1c	1 or 2 ovaries w/ capsule ruptured, ovarian surface tumor, or malignant cells in ascites/peritoneal wash
	T2	**Tumor involves 1 or 2 ovaries w/ pelvic extension**
	T2a	Extension/implants on uterus/tubes w/ no malignant cells in ascites/peritoneal washings
	T2b	Extension/implants on other pelvic tissues w/ no malignant cells in ascites/peritoneal washings
	T2c	Pelvic extension and/or implants (T2a/b) w/ malignant cells in ascites/peritoneal washings
	T3	**Tumor involves 1 or 2 ovaries w/ microscopically confirmed peritoneal metastases outside pelvis**
	T3a	Microscopic peritoneal metastasis beyond pelvis (no macroscopic tumor)
	T3b	Macroscopic peritoneal metastases beyond pelvic ≤2 cm in greatest dimension
	T3c	Peritoneal metastasis beyond pelvis >2 cm in greatest dimension and/or regional lymph node metastasis
Regional Lymph Nodes (N)	Nx	Regional lymph nodes cannot be assessed
	N0	No regional lymph node metastasis
	N1	**Regional lymph node metastasis**
Distant Metastasis (M)	M0	No distant metastases
	M1	**Distant metastasis (excludes peritoneal)**

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National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Ovarian Cancer; v2.2017.

Staging

Stage	T	N	M
IA	T1a	N0	M0
IB	T1b	N0	M0
IC	T1c	N0	M0
IIA	T2a	N0	M0
IIB	T2b	N0	M0
IIC	T2c	N0	M0
IIIA	T3a	N0	M0
IIIB	T3b	N0	M0
IIIC	T3c	N0	M0
	Any T	N1	M0
IV	Any T	Any N	M1

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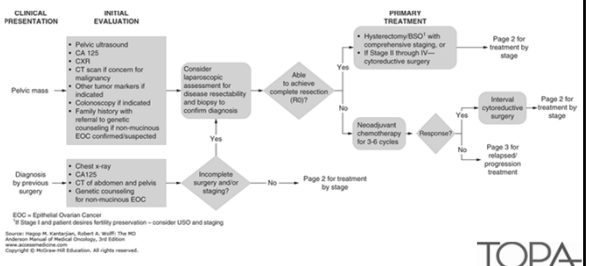
National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Ovarian Cancer; v2.2017.

Clinical Work Up and Primary Treatment



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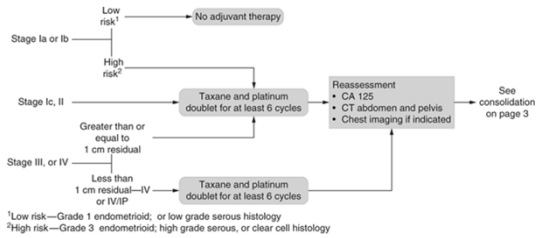
USO: unilateral salpingo-oophorectomy
BSO: bilateral salpingo-oophorectomy

Primary Adjuvant Treatment



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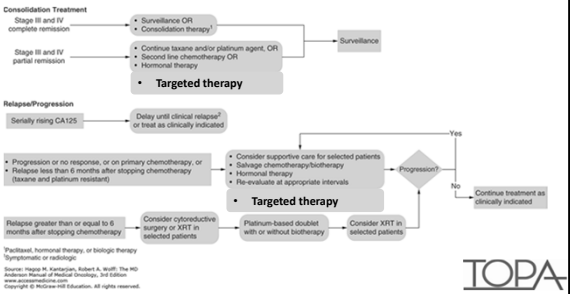
Consolidation/Recurrent Disease Treatment



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PARP Inhibitors

Olaparib
Rucaparib
Niraparib

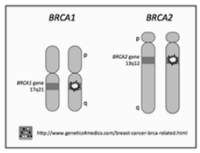
What is PARP?

- Poly (ADP-ribose) polymerase (PARP) enzymes
- Family of 18 proteins which repair single-stranded DNA damage via:
  - Base-excision repair
  - Inhibition of the non-homologous end-joining DNA repair pathway (a method of double-strand break repair)
- Inhibition of the PARP1 and PARP2 enzymes results in the accumulation of double-stranded breaks, which are typically repaired by the homologous recombination double-stranded DNA repair pathway

Swisher EM et al. *Lancet Oncol*. 2017;18(1):75-87.
Dziadkowiec KN et al. *Prz Menopauzalny*. 2016;15(4):215-219.

Why PARP Inhibitors?

- *BRCA1* and *BRCA2* enzymes repair double-stranded DNA breaks via homologous recombination
  - A germline or somatic mutation in one *BRCA1/2* allele can be compensated for by the remaining wild-type allele
  - Loss of the remaining wild-type allele, known as loss of heterozygosity (LOH), renders the homologous recombination pathway ineffective
- Tumor cells which have LOH are therefore most susceptible to PARP inhibition, as they have no mechanism to repair double-stranded breaks



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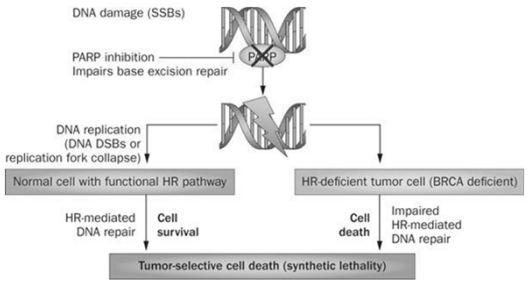


Banerjee S et al. *Nat Rev Clin Oncol*. 2010;7(9):508-19.

Olaparib (Lynparza®)

- Granted accelerated approval on December 19, 2014
- Initial indication:
  - Olaparib capsules as monotherapy for patients with deleterious or suspected deleterious germline BRCA mutated recurrent ovarian cancer who were previously treated with ≥3 prior lines of chemotherapy
- Approved with BRACAnalysis CDx, a diagnostic test which detects BRCA mutations

Lynparza™ (olaparib) [prescribing information].

Olaparib for Recurrent Disease

- Multicenter, single arm, phase II trial
  - Enrolled patients with a *gBRCA1/2* mutation and recurrent ovarian, breast, pancreatic, or prostate cancer
  - Patients received olaparib 400 mg BID until disease progression or unacceptable toxicity
- 298 patients enrolled → 193 patients with ovarian cancer resistant to prior platinum-based therapy or unsuitable for further platinum chemotherapy
- Tumor response rate
  - 31.1% in patients with ovarian cancer (95% CI, 24.6-38.1)
  - Did not differ based on *BRCA1* vs *BRCA2* mutation

Kaufman B et al. *J Clin Oncol*. 2015;33(3):244-50.

Olaparib for Recurrent Disease

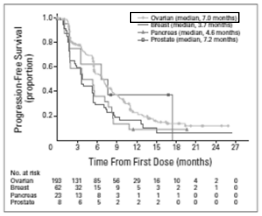


Fig 1. Progression-free survival.

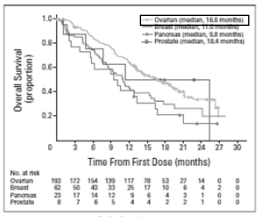


Fig 2. Overall survival.

Kaufman B et al. *J Clin Oncol*. 2015;33(3):244-50.

Olaparib for Recurrent Disease

Table 4. Any-Grade AEs Reported in > 15% of Patients Overall or Grade ≥ 3 AEs Reported in > 5% of Patients Overall

	Ovarian (n = 193)				Breast (n = 62)				Pancreas (n = 23)				Prostate (n = 8)				Other (n = 12)				Total (N = 298)			
	Any Grade		Grade ≥ 3		Any Grade		Grade ≥ 3		Any Grade		Grade ≥ 3		Any Grade		Grade ≥ 3		Any Grade		Grade ≥ 3		Any Grade		Grade ≥ 3	
AE	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Fatigue	116	60.1	12	6.2	30	48.4	3	4.8	17	73.9	3	13.0	1	12.5	0	0.0	12	100.0	1	8.3	176	59.1	19	6.4
Nausea	119	61.7	1	0.5	33	53.2	0	0.0	11	47.8	0	0.0	3	37.5	0	0.0	10	83.3	0	0.0	176	59.1	1	0.3
Vomiting	75	38.9	5	2.6	21	33.9	1	1.6	9	39.1	1	4.3	0	0.0	0	0.0	6	50.0	0	0.0	111	37.2	7	2.3
Anemia	62	32.1	36	18.7	16	25.8	9	14.5	9	39.1	4	17.4	5	62.5	1	12.5	6	50.0	2	16.7	98	32.9	52	17.4
Diarrhea	56	29.0	3	1.6	11	17.7	1	1.6	7	30.4	0	0.0	3	37.5	0	0.0	4	33.3	0	0.0	81	27.2	4	1.3
Abdominal pain	58	30.1	14	7.3	5	8.1	1	1.6	7	30.4	1	4.3	0	0.0	0	0.0	7	58.3	1	8.3	77	25.8	17	5.7
Decreased appetite	36	18.7	1	0.5	17	27.4	0	0.0	4	17.4	0	0.0	2	25.0	0	0.0	3	25.0	0	0.0	62	20.8	1	0.3
Dyspepsia	38	19.7	0	0.0	9	14.5	0	0.0	2	8.7	0	0.0	0	0.0	0	0.0	3	25.0	0	0.0	52	17.4	0	0.0
Headache	32	16.6	0	0.0	14	22.6	1	1.6	1	4.3	0	0.0	0	0.0	0	0.0	1	8.3	0	0.0	48	16.1	1	0.3
Dysgeusia	39	20.2	0	0.0	4	6.5	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0	3	25.0	0	0.0	47	15.8	0	0.0

Abbreviation: AE, adverse event.

Kaufman B et al. *J Clin Oncol*. 2015;33(3):244-50.

Maintenance Olaparib

- Olaparib tablets granted regular approval on August 17, 2017
- Indication:
  - Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy
  - Monotherapy for patients with deleterious or suspected deleterious germline BRCA mutated recurrent ovarian cancer who were previously treated with three or more prior lines of chemotherapy
- As the tablets also received approval for the initial indication of recurrent disease, the capsules will be phased out and will only be available through Lynparza Specialty Pharmacy Network

US FDA Website. https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm572143.htm.

Maintenance Olaparib

Study 19

- Randomized, double-blind, placebo-controlled, phase II trial
- Maintenance olaparib in patients in partial/complete response to most recent platinum-based therapy (≥2 platinum therapies)
- 265 patients randomized 1:1 to olaparib (capsules) 400 mg BID vs placebo
- Median PFS: 8.4 vs 4.8 months (p<0.001)

SOLO-2

- Randomized, double-blind, placebo-controlled, phase III trial
- Maintenance olaparib in patients with a *BRCA1/2* mutation in at least partial response to most recent platinum-based therapy (≥2 platinum therapies)
- 295 patients randomized 2:1 to olaparib 300 mg (tablet) BID vs placebo
- Median PFS: 19.1 vs 5.5 months (p<0.0001)

Ledermann J et al. *N Engl J Med*. 2012;366(15):1382-92.
Pujade-Lauraine E et al. 2017 Society of Gynecologic Oncologists Annual Meeting. Abstract LBA2.

Olaparib

	Capsule	Tablet
Dosage Form	50 mg (to be phased out)	100, 150 mg
Indication/Dosing	Recurrence: 400 mg PO BID	Maintenance: 300 mg PO BID Recurrence: 300 mg PO BID
Administration	With or without food	With or without food
Emetic Risk	Moderate	Moderate
Dose Reductions: Concomitant Therapy	CYP3A4 inhibitors: moderate (200 mg BID) or strong (150 mg BID)	CYP3A4 inhibitors: moderate (150 mg BID) or strong (100 mg BID)
Dose Reductions: Renal	CrCl 31-50 mL/min: 300 mg BID	CrCl 31-50 mL/min: 200 mg BID
Dose Reductions: Toxicity	1st reduction: 200 mg BID 2nd reduction: 100 mg BID	1st reduction: 250 mg BID 2nd reduction: 200 mg BID
Storage	Room temperature	Room temperature

Lynparza™ (olaparib) [prescribing information].

Rucaparib (Rubraca®)

- Granted accelerated approval on December 19, 2016
- Indication:
  - Treatment of patients with deleterious *BRCA* mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with ≥2 prior lines of chemotherapy
- Approved with FoundationFocus CDx_{BRCA}, a next-generation sequencing diagnostic that detects alterations in the *BRCA1/2* genes

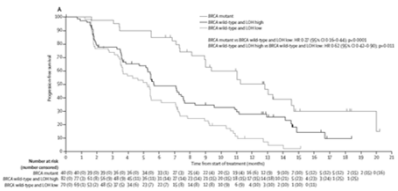
US FDA Website. https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm533891.htm.

ARIEL2 Part 1

- 2-part, phase II, open-label trial
- Rucaparib in patients with recurrent, platinum-sensitive, high-grade ovarian carcinoma with or without a *BRCA* mutation
  - 3 subgroups: deleterious germline/somatic *BRCA* mutant, *BRCA* wild-type + LOH high, or *BRCA* wild-type + LOH low
- 206 patients received rucaparib 600 mg BID for continuous 28 day cycles

Swisher EM et al. *Lancet Oncol*. 2017;18(1):75-87.

ARIEL2 Part 1



Median PFS:
BRCA mutant: 12.8 months (95% CI 9.0-14.7, p<0.0001 compared to LOH low)
LOH high: 5.7 months (95% CI 5.3-7.6, p=0.011 compared to LOH low)
LOH low: 5.2 months (95% CI 3.6-5.5)

Swisher EM et al. *Lancet Oncol*. 2017;18(1):75-87.

ARIEL2 Part 1

	Grade 1–2	Grade 3	Grade 4	Grade 5
Nausea	154 (75%)	9 (4%)	0	0
Asthenia or fatigue	141 (69%)	18 (9%)	0	0
Constipation	91 (45%)	3 (1%)	0	0
Vomiting	85 (42%)	4 (2%)	0	0
Dysgeusia	87 (42%)	0	0	0
Alanine aminotransferase or aspartate aminotransferase increased*	61 (30%)	24 (12%)	1 (<1%)	0
Decreased appetite	80 (39%)	4 (2%)	0	0
Anaemia; decreased haemoglobin	29 (14%)	43 (21%)	2 (1%)	0
Diarrhoea	61 (30%)	7 (3%)	0	0
Abdominal pain	55 (27%)	5 (2%)	0	0
Dyspnoea	45 (22%)	1 (<1%)	0	0
Abdominal distension	43 (21%)	0	0	0
Dizziness	37 (18%)	1 (<1%)	0	0
Urinary tract infection	33 (16%)	4 (2%)	0	0
Blood creatinine increased	34 (17%)	0	0	0
Headache	34 (17%)	0	0	0
Cough	33 (16%)	0	0	0
Back pain	30 (15%)	2 (1%)	0	0
Thrombocytopenia; platelet count decreased	25 (12%)	5 (2%)	0	0
Photosensitivity reaction	27 (13%)	0	0	0
Neutropenia; neutrophil count decreased	10 (5%)	9 (4%)	7 (3%)	0
Insomnia	25 (12%)	0	0	0
Pyrexia	24 (12%)	1 (<1%)	0	0
Abdominal pain (upper)	22 (11%)	0	0	0
Oedema peripheral	22 (11%)	0	0	0
Alopecia	21 (10%)	0	0	0
Stomatitis	20 (10%)	1 (<1%)	0	0
Upper respiratory tract infection	21 (10%)	0	0	0

Swisher EM et al. *Lancet Oncol*. 2017;18(1):75-87.

Rucaparib

- Dosage form
  - 200, 250, 300 mg tablets
- Dosing
  - Recurrent: 600 mg PO BID with or without food
  - Moderate emetic risk!
- Dose reductions
  - No renal or hepatic dose reductions required
  - Toxicity
    - 1st dose reduction: 500 mg BID
    - 2nd dose reduction: 400 mg BID
    - 3rd dose reduction: 300 mg BID
- Substrate of BRCP, P-glycoprotein, CYP1A2 (minor), CYP2D6 (minor), CYP3A4 (minor)
- Store at room temperature

Rubraca™ (rucaparib) [prescribing information].

Niraparib (Zejula®)

- Granted regular approval on March 27, 2017
- Indication:
  - Maintenance treatment of patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in complete or partial response to platinum-based chemotherapy

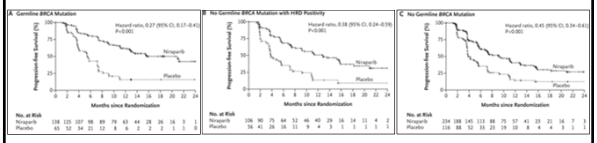
US FDA Website. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm548487.htm.

ENGOT-OV16/NOVA

- Randomized, double-blind, phase III trial
- Niraparib for patients with platinum-sensitive recurrent ovarian cancer in complete or partial response following platinum-based therapy
  - 2 cohorts: *gBRCA* mutation (homologous recombination deficiency [HRD] or non-HRD) and no *gBRCA* mutation
- 553 patients randomized 2:1 to niraparib 300 mg daily vs placebo

Mirza MR et al. *N Engl J Med*. 2016;375(22):2154-2164.

ENGOT-OV16/NOVA



Median PFS: 21.0 vs 5.5 months | Median PFS: 12.9 vs 3.8 months | Median PFS: 9.3 vs 3.9 months

Mirza MR et al. *N Engl J Med*. 2016;375(22):2154-2164.

ENGOT-OV16/NOVA

Table 2. Adverse Events.*

Event	Niraparib (N = 367)		Placebo (N = 179)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Nausea	270 (73.6)	11 (3.0)	63 (35.2)	2 (1.1)
Thrombocytopenia†	225 (61.3)	124 (33.8)	10 (5.6)	1 (0.6)
Fatigue‡	218 (59.4)	30 (8.2)	74 (41.3)	1 (0.6)
Anemia§	184 (50.1)	93 (25.3)	12 (6.7)	0
Constipation	146 (39.8)	2 (0.5)	36 (20.1)	1 (0.6)
Vomiting	126 (34.3)	7 (1.9)	29 (16.2)	1 (0.6)
Neutropenia¶	111 (30.2)	72 (19.6)	11 (6.1)	3 (1.7)
Headache	95 (25.9)	1 (0.3)	17 (9.5)	0
Decreased appetite	93 (25.3)	1 (0.3)	26 (14.5)	1 (0.6)
Insomnia	89 (24.3)	1 (0.3)	13 (7.3)	0
Abdominal pain	83 (22.6)	4 (1.1)	53 (29.6)	3 (1.7)
Dyspnea	71 (19.3)	4 (1.1)	15 (8.4)	2 (1.1)
Hypertension	71 (19.3)	30 (8.2)	8 (4.5)	4 (2.2)
Diarrhea	70 (19.1)	1 (0.3)	37 (20.7)	2 (1.1)
Dizziness	61 (16.6)	0	13 (7.3)	0
Cough	55 (15.0)	0	8 (4.5)	0
Back pain	49 (13.4)	2 (0.5)	21 (11.7)	0
Arthralgia	43 (11.7)	1 (0.3)	22 (12.3)	0
Dyspepsia	42 (11.4)	0	17 (9.5)	0
Nasopharyngitis	41 (11.2)	0	13 (7.3)	0
Urinary tract infection	38 (10.4)	3 (0.8)	11 (6.1)	2 (1.1)
Palpitations	38 (10.4)	0	3 (1.7)	0
Dysgeusia	37 (10.1)	0	7 (3.9)	0
Myalgia	30 (8.2)	1 (0.3)	18 (10.1)	0
Abdominal distention	28 (7.6)	0	22 (12.3)	1 (0.6)

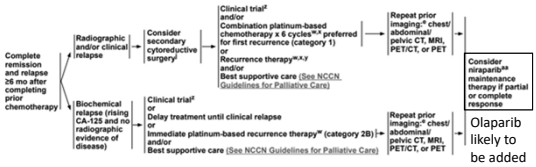
Mirza MR et al. *N Engl J Med*. 2016;375(22):2154-2164.

Niraparib

- Dosage form
  - 100 mg capsule
- Dosing
  - Maintenance: 300 mg PO daily with or without food
  - Low emetic risk
- Dose adjustments
  - No renal or hepatic dose reductions required
  - Toxicity (hematologic or non-hematologic)
    - First dose reduction: 200 mg daily
    - Second dose reduction: 100 mg daily
    - Discontinue if <100 mg daily is required
- Substrate of BCRP, P-glycoprotein; inhibits BCRP
- Store at room temperature

Zejula™ (niraparib) [prescribing information].

PARP Inhibitors: Where are we now?



Olaparib likely to be added

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Ovarian Cancer; v2.2017.

PARP Inhibitors: Where are we now?

Acceptable Recurrence Therapies for Epithelial (including LCOHP)/Fallopian Tube/Primary Peritoneal Cancer[ff]

	Cytotoxic Therapy (In alphabetical order)*		Targeted Therapy*
Preferred Agents	**Platinum-Sensitive Disease**[jj] Carboplatin[l] Carboplatin/docetaxel[2,3] Carboplatin/gemcitabine[t] Carboplatin/gemcitabine/bevacizumab[k,l,m,4] Carboplatin/liposomal doxorubicin[n] (category 1) Carboplatin/paclitaxel, albumin bound (for patients with confirmed taxane hypersensitivity) Carboplatin/paclitaxel (category 1)[5] Carboplatin/paclitaxel (weekly)[7] Cisplatin[6] Cisplatin/gemcitabine[8] **Additional options for mucinous carcinoma only:** 5-FU/leucovorin/oxaliplatin ± bevacizumab (category 2B for bevacizumab)[k,l] Capecitabine + oxaliplatin	**Platinum-Resistant Disease** Docetaxel[9] Etoposide, oral[10] Gemcitabine[11,12] Liposomal doxorubicin[11,12] Liposomal doxorubicin/bevacizumab[k,l,13] Paclitaxel (weekly)[14] ± pazopanib[15] Paclitaxel (weekly)/bevacizumab[k,l,13] Topotecan[16,17] Topotecan/bevacizumab[k,l,13]	**Single Agents** Bevacizumab[k,l,18,19] Olaparib[h,20,21] Rucaparib[h,24] (platinum-resistant disease)

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Ovarian Cancer; v2.2017.

PARP Inhibitors: Where are we now?

Acceptable Recurrence Therapies for Epithelial (including LCOHP)/Fallopian Tube/Primary Peritoneal[ff]

	Cytotoxic Therapy (In alphabetical order)*	Hormonal Therapy*	Targeted Therapy*	Radiation Therapy*
Other Potentially Active Agents	**Single Agents**[h,22] Altretamine Capecitabine Cyclophosphamide Doxorubicin Ifosfamide Irinotecan Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound Pemetrexed Vinorelbine **Combinations** Carboplatin/paclitaxel/bevacizumab[k,l,m] (platinum-sensitive disease)	Aromatase inhibitors Leuprolide acetate Megestrol acetate Tamoxifen	Pazopanib (category 2B)[23] Rucaparib[h,24] (platinum-sensitive disease)	Palliative localized radiation therapy

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Ovarian Cancer; v2.2017.

Summary

	Olaparib	Rucaparib	Niraparib
Dosage Form	50 mg capsule 100, 150 mg tablet	200, 250, 300 mg tablet	100 mg capsule
Indication	Recurrent ovarian Maintenance for ovarian, fallopian tube, or primary peritoneal	Recurrent ovarian	Maintenance for ovarian, fallopian tube, or primary peritoneal
Dosing	Recurrence: 400 mg BID Maintenance: 300 mg BID	Recurrence: 600 mg BID	Maintenance: 300 mg QD
Administration	With or without food	With or without food	With or without food
Emetic Risk	Moderate	Moderate	Low
Dose Reductions	3A4 inhibitor CrCl ≤ 50 ml/min No hepatic adj Toxicity	No renal/hepatic adj Toxicity	No renal/hepatic adj Toxicity
Storage	Room temperature	Room temperature	Room temperature

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Future Directions

Current PARP Inhibitors
New PARP Inhibitors

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Future Directions: Current PARP Inhibitors

- Rucaparib
  - ARIEL3: maintenance therapy for platinum-sensitive, high-grade serous or endometrioid epithelial ovarian, primary peritoneal or fallopian tube cancer
  - ARIEL4: phase III study of rucaparib vs. chemotherapy for relapsed, *BRCA* mutant, high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer
  - Ovarian cancer (+ anti-PDL1)
- Niraparib
  - Ovarian cancer (+ anti-PD1)
  - Recurrent ovarian cancer

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ClinicalTrials.gov: NCT01968213.
ClinicalTrials.gov: NCT02855944.
National Institutes of Health: ClinicalTrials.gov.

Future Directions: New PARP Inhibitors

- Talazoparib
  - Ovarian cancer after prior PARP exposure
  - Ovarian cancer recurrence
- Veliparib
  - Ovarian cancer (+ topotecan)
  - Ovarian cancer (+ carboplatin/paclitaxel)
  - Ovarian cancer (+ liposomal doxorubicin/carboplatin/bevacizumab)
  - Ovarian cancer maintenance
  - Ovarian cancer recurrence

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National Institutes of Health: ClinicalTrials.gov.

Conclusions

- Ovarian cancer remains a malignancy with a poor prognosis, particularly if diagnosed at a later stage
- PARP inhibition represents a novel treatment strategy for ovarian cancer, both in the recurrent and maintenance setting
- Further research into use of PARP inhibitors may change the landscape of treatment of ovarian cancer, and allow for potentially more treatment options

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Reminder…

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An Update on Ovarian Cancer with a Focus on PARP Inhibitors

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