Taipei Veterans General Hospital

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## Sample Information

**Patient Name:** 姚穎潔
**Gender:** Female
**ID No.:** M221939170
**History No.:** 42858888
**Age:** 39

**Ordering Doctor:** DOC3697E 陳怡仁
**Ordering REQ.:** 0CPLMTA
**Signing in Date:** 2023/08/17

**Path No.:** M112-00223
**MP No.:** BR23059
**Assay:** Oncomine BRCA1/2 Assay
**Sample Type:** FFPE
**Block No.:** S112-31605G
**Percentage of tumor cells:** 80%

**Reporting Doctor:** DOC5424G 彭昱璟 (Phone: 8#5424)

**Note:**

## Sample Cancer Type: Ovarian Cancer



### Report Highlights

1 Relevant Biomarkers
7 Therapies Available
1 Clinical Trials

## Relevant Ovarian Cancer Variants

| Gene | Finding |
|---|---|
| BRCA1 | ***BRCA1 p.(C328*) c.981_982delAT (HR Deficient)*** |
| BRCA2 | None detected |

## Relevant Biomarkers

| Tier | Genomic Alteration | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|---|---|---|---|---|
| **IA** | *BRCA1 p.(C328*) c.981_982delAT*<br>HR Deficient<br>BRCA1 DNA repair associated<br>Allele Frequency: 89.78% | **bevacizumab + olaparib** [1, 2]<br>**olaparib** [1, 2]<br>**olaparib + hormone therapy** [1]<br>**rucaparib** [1]<br>niraparib | **abiraterone + niraparib** [2]<br>**bevacizumab + olaparib** [1, 2]<br>**olaparib** [1, 2]<br>**olaparib + hormone therapy** [1]<br>**rucaparib** [1]<br>talazoparib | 1 |

**Public data sources included in relevant therapies: FDA**[1], NCCN, **EMA**[2], ESMO

# Variant Details

## DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Locus | Allele Frequency | Transcript | Variant Effect | ClinVar[1] | Coverage |
|---|---|---|---|---|---|---|---|---|
| BRCA1 | p.(C328*) | c.981_982delAT | chr17:41246565 | 89.78% | NM_007294.4 | nonsense | Pathogenic | 1977 |
| BRCA2 | p.(V1269=) | c.3807T>C | chr13:32912299 | 35.85% | NM_000059.3 | synonymous | Benign | 2000 |
| BRCA2 | p.(L1521=) | c.4563A>G | chr13:32913055 | 100.00% | NM_000059.3 | synonymous | Benign | 1989 |
| BRCA2 | p.(V2171=) | c.6513G>C | chr13:32915005 | 100.00% | NM_000059.3 | synonymous | Benign | 1999 |
| BRCA2 | p.(V2466A) | c.7397T>C | chr13:32929387 | 99.90% | NM_000059.3 | missense | Benign | 1999 |
| BRCA1 | p.(S1613G) | c.4837A>G | chr17:41223094 | 86.63% | NM_007294.4 | missense | Benign | 1997 |
| BRCA1 | p.(S1436=) | c.4308T>C | chr17:41234470 | 88.60% | NM_007294.4 | synonymous | Benign | 2000 |
| BRCA1 | p.(K1183R) | c.3548A>G | chr17:41244000 | 88.50% | NM_007294.4 | missense | Benign | 2000 |
| BRCA1 | p.(E1038G) | c.3113A>G | chr17:41244435 | 89.75% | NM_007294.4 | missense | Benign | 2000 |
| BRCA1 | p.(P871L) | c.2612C>T | chr17:41244936 | 87.24% | NM_007294.4 | missense | Benign | 1998 |
| BRCA1 | p.(L771=) | c.2311T>C | chr17:41245237 | 86.79% | NM_007294.4 | synonymous | Benign | 1999 |
| BRCA1 | p.(S694=) | c.2082C>T | chr17:41245466 | 88.34% | NM_007294.4 | synonymous | Benign | 1999 |

[1] Based on Clinvar version 20200329

# Biomarker Descriptions

**BRCA1 (BRCA1 DNA repair associated)**

Background: The breast cancer early onset gene 1 (BRCA1) encodes one of two BRCA proteins (BRCA1 and BRCA2) initially discovered as major hereditary breast cancer genes. Although structurally unrelated, both BRCA1 and BRCA2 exhibit tumor suppressor function and are integrally involved in the homologous recombination repair (HRR) pathway, a pathway critical in the repair of damaged DNA[1,2]. Specifically, BRCA1/2 are required for the repair of chromosomal double strand breaks (DSBs) which are highly unstable and compromise genome integrity[1,2]. Inherited pathogenic mutations in BRCA1/2 are known to confer increased risk in women for breast and ovarian cancer and in men for breast and prostate cancer[3,4,5]. For individuals diagnosed with inherited pathogenic or likely pathogenic BRCA1/2 variants, estimated lifetime risks range from 41% to 90% for developing breast cancer and 8 to 62% for developing ovarian cancer[6].

Alterations and prevalence: Inherited BRCA1/2 mutations occur in 1:400 to 1:500 individuals and are observed in 10-15% of ovarian cancer, 5-10% of breast cancer, and 1-4% of prostate cancer[7,8,9,10,11,12,13,14]. Somatic alterations in BRCA1 are observed in 5-10% of uterine corpus endometrial carcinoma, cutaneous melanoma, bladder urothelial carcinoma, diffuse large B-cell lymphoma, and cervical squamous cell carcinoma, 3-4% of lung squamous cell carcinoma, lung adenocarcinoma, stomach adenocarcinoma, ovarian serous cystadenocarcinoma, colorectal adenocarcinoma, and breast invasive carcinoma, and 2% of head and neck squamous cell carcinoma and glioblastoma multiforme[15,16].

Potential relevance: Individuals possessing BRCA1/2 pathogenic germline or somatic mutations are shown to exhibit sensitivity to platinum based chemotherapy as well as treatment with poly (ADP-ribose) polymerase inhibitors (PARPi)[17]. Inhibitors targeting PARP induce synthetic lethality in recombination deficient BRCA1/2 mutant cells[18,19]. Consequently, several PARP inhibitors have been FDA approved for BRCA1/2-mutated cancers. Olaparib[20] (2014) was the first PARPi to be approved by the FDA for BRCA1/2 aberrations. Originally approved for the treatment of germline variants, olaparib is now indicated (2018) for the maintenance treatment of both germline BRCA1/2-mutated (gBRCAm) and somatic BRCA1/2-mutated (sBRCAm) epithelial ovarian, fallopian tube, or primary peritoneal cancers that are responsive to platinum-based chemotherapy. Olaparib is also indicated for the treatment of patients with gBRCAm HER2-negative metastatic breast cancer and metastatic pancreatic adenocarcinoma. Additionally, olaparib[20] is approved (2020) for metastatic castration-resistant prostate cancer (mCRPC) with deleterious or suspected deleterious, germline or somatic mutations in HRR genes that includes BRCA1. Rucaparib[21] is also approved (2020) for deleterious gBRCAm or sBRCAm mCRPC. Talazoparib[22] (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Niraparib[23] (2017) is another PARPi approved for the treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancers with

## Biomarker Descriptions (continued)

a deleterious or suspected deleterious BRCA mutation. Despite tolerability and efficacy, acquired resistance to PARP inhibition has been clinically reported[24]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[25]. In addition to PARP inhibitors, other drugs which promote synthetic lethality have been investigated for BRCA mutations. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[26], for BRCA1/2, PALB2, or other homologous recombination deficiency (HRD) mutations in breast and ovarian cancers. Like PARPi, pidnarulex promotes synthetic lethality but through an alternative mechanism which involves stabilization of G-quadruplexes at the replication fork leading to DNA breaks and genomic instability.

**HR Deficient**

Background: Homologous recombination repair (HRR) is a DNA repair mechanism that targets double stranded breaks (DSBs) and interstrand cross-links (ICL) in DNA[27]. Homologous recombination deficiency (HRD) is characterized by the cell's inability to repair these DSBs[27,28]. HRD is caused by genetic or epigenetic alterations in the HRR pathway genes, most notably BRCA1 and BRCA2 along with other genes such as ATM and PALB2[29,30,31,32]. A consequence of HRD due to the failure to repair DSBs is genomic instability[33,34]. Genomic instability is an increased tendency towards acquiring genomic alterations during cell division[35,36,37,38,39,40]. These alterations include small structural variations (i.e., single nucleotide variants (SNVs), insertions, and deletions) as well as significant structural variations (i.e., loss or gain of large chromosome fragments)[36,41,42]. Variations of genomic instability include chromosomal instability, intrachromosomal instability, microsatellite instability, and epigenetic instability[35]. Importantly, while the impact of frame-shift mutations in specific HRR genes can be mitigated by secondary mutations that restore the correct reading frame and thereby alleviate HRD, the effects of genomic instability are permanent and not reversible[43,44,45]. For this reason, the alterations characteristic of genomic instability are referred to as genomic scars[46,47]. Some of the genomic scar signatures that are characteristic of the HRD phenotype include loss of heterozygosity (LOH), telomeric allelic imbalance (TAI), and large-scale transition (LST)[27,48]. Current methods for HRD detection are heterogeneous and the definition for HRD positive tumors varies depending on the cancer type[27]. Generally, these methods detect the causes of HRD (i.e., alterations in HRR genes) and/or the consequences (i.e., signatures of genomic instability/genomic scarring)[27,33,49,50].

Alterations and prevalence: In a pan-cancer analysis of HRR gene mutations and genomic scar signatures in 8847 tumors across 33 cancer types, 17.5% of tumors were HRD-positive and 4% of tumors were positive for the BRCA1/2 mutation[51]. Specifically, HRD-positive status was observed in over 50% of ovarian serous cystadenocarcinoma and lung squamous cell carcinoma, 35-45% of esophageal carcinoma, uterine carcinosarcoma, sarcoma, and lung adenocarcinoma, 20-30% of stomach adenocarcinoma, bladder urothelial carcinoma, breast invasive carcinoma, and head and neck squamous cell carcinoma, 5-15% of endometrial cancer, mesothelioma, cervical cancer, pancreatic adenocarcinoma, cutaneous melanoma, hepatocellular carcinoma, diffuse large B-cell lymphoma, and adrenocortical carcinoma, and 1-4% of rectum adenocarcinoma, prostate adenocarcinoma, colon adenocarcinoma, testicular germ cell tumors, kidney chromophobe, glioblastoma multiforme, low grade glioma, and renal clear cell carcinoma[51]. Inherited BRCA1/2 mutations occur in 1:400 to 1:500 individuals and are observed in 10-15% of ovarian cancer, 5-10% of breast cancer, and 1-4% of prostate cancer[7,8,9,10,11,12,13,14]. Somatic alterations in BRCA1 are observed in 5-10% of uterine corpus endometrial carcinoma, cutaneous melanoma, bladder urothelial carcinoma, diffuse large B-cell lymphoma, and cervical squamous cell carcinoma, 3-4% of lung squamous cell carcinoma, lung adenocarcinoma, stomach adenocarcinoma, ovarian serous cystadenocarcinoma, colorectal adenocarcinoma, and breast invasive carcinoma, and 2% of head and neck squamous cell carcinoma and glioblastoma multiforme[15,16]. Somatic alterations in BRCA2 are observed in 5-15% of uterine corpus endometrial carcinoma, cutaneous melanoma, bladder urothelial carcinoma, stomach adenocarcinoma, colorectal adenocarcinoma, lung squamous cell carcinoma, lung adenocarcinoma, and uterine carcinosarcoma, 3-4% of cervical squamous cell carcinoma, head and neck squamous cell carcinoma, esophageal adenocarcinoma, ovarian serous cystadenocarcinoma, cholangiocarcinoma, breast invasive carcinoma, renal papillary cell carcinoma, and 2% of renal clear cell carcinoma, hepatocellular carcinoma, thymoma, prostate adenocarcinoma, sarcoma, and glioblastoma multiforme[15,16].

Potential relevance: HRD status is an important biomarker in advanced ovarian and prostate cancer because it predicts response to certain treatments including poly-ADP ribose polymerase (PARP) inhibitors and platinum chemotherapies[5,52,53]. Disruption of HRR or inhibition of PARP, are tolerated by cells through the utilization of complementary DNA repair pathways. However, presence of HRD and subsequent treatment with PARP inhibitors block DNA repair, causing accumulation of DNA damage and cell death through synthetic lethality[27,54,55,56]. Several PARP inhibitors are approved by the FDA for various cancers associated with markers of HRD. Olaparib[20] was the first PARP inhibitor originally approved in 2014 for ovarian cancer with germline mutations in BRCA1/2 (gBRCAm). The utility of olaparib has since expanded to include genomic instability markers and mutations in other HRR genes. Specifically, olaparib as monotherapy is now indicated for gBRCAm and somatic BRCA1/2 mutated (sBRCAm) ovarian cancer and in combination with bevacizumab for BRCA1/2 mutated or genomic instability positive ovarian cancer[20]. In addition, olaparib is approved in prostate cancer with germline or somatic mutations in HRR genes including ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L[20,30,57]. Olaparib is also approved for gBRCAm HER2 negative breast cancer and as maintenance therapies for gBRCAm pancreatic cancers[20]. Other PARP inhibitors that are FDA approved for BRCA mutated cancers include rucaparib[21] (2016) that is indicated for gBRCAm or sBRCAm ovarian and prostate cancers, niraparib[23] (2017) that is indicated for gBRCAm ovarian cancer, and talazoparib[22] (2018) that is indicated for gBRCAm HER2-negative metastatic breast cancer. Niraparib is also recommended for the treatment of HRD-positive ovarian cancer, defined by BRCA1/2 mutations and/or genomic instability[58]. In addition to PARP inhibitors, other drugs which promote synthetic lethality have been investigated for BRCA1/2 mutations. In 2022, the

## Biomarker Descriptions (continued)

FDA granted fast track designation to the small molecule inhibitor, pidnarulex[26], for BRCA1/2, PALB2, or other HRR gene mutations in breast and ovarian cancers. Like PARP inhibitors, pidnarulex[26] causes synthetic lethality but through an alternative mechanism which involves stabilization of G-quadruplexes at the replication fork leading to DNA breaks and genomic instability. Despite tolerability and efficacy, acquired resistance to PARP inhibitors such as olaparib has been clinically reported[24]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[25]. Other potential mechanisms of resistance to PARP inhibitors include restoration of HRR activity, stabilization of the replication forks, inhibition of PARP trapping, increased drug efflux mediated by P-glycoprotein, and cell cycle control alterations[25,59,60,61].

## Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### BRCA1 p.(C328*) c.981_982delAT

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| olaparib | ◑ | ◑ | ◑ | ◑ | ✖ |
| rucaparib | ◑ | ◑ | ✖ | ● | ✖ |
| bevacizumab + olaparib | ◑ | ● | ◑ | ● | ✖ |
| olaparib + abiraterone acetate + prednisolone | ◑ | ✖ | ✖ | ✖ | ✖ |
| olaparib + abiraterone acetate + prednisone | ◑ | ✖ | ✖ | ✖ | ✖ |
| niraparib | ✖ | ● | ✖ | ● | ✖ |
| abiraterone + niraparib | ✖ | ✖ | ○ | ✖ | ✖ |
| talazoparib | ✖ | ✖ | ✖ | ○ | ✖ |
| senaparib, IMP-9064 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

# Relevant Therapy Details

## Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

FDA information is current as of 2023-06-14. For the most up-to-date information, search www.fda.gov.

## BRCA1 p.(C328*) c.981_982delAT

### ◑ olaparib, bevacizumab + olaparib, olaparib + abiraterone acetate + prednisolone, olaparib + abiraterone acetate + prednisone

**Cancer type:** Castration-Resistant Prostate Cancer, Ovarian Cancer **Label as of:** 2023-05-31 **Variant class:** BRCA1 mutation

**Indications and usage:**

LYNPARZA® is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

Ovarian cancer

- for the 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. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.
- in combination with bevacizumab for the 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 homologous recombination deficiency (HRD)-positive status defined by either:
  - a deleterious or suspected deleterious BRCA mutation, and/or
  - genomic instability.

Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.

Breast cancer

- for the adjuvant treatment of adult patients with deleterious or suspected deleterious gBRCAm human epidermal growth factor receptor 2 (HER2)-negative high risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.
- for the treatment of adult patients with deleterious or suspected deleterious gBRCAm, HER2-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

Pancreatic cancer

- for the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

Prostate cancer

- for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.
- in combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC). Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208558s025lbl.pdf

## BRCA1 p.(C328*) c.981_982delAT (continued)

### rucaparib

**Cancer type:** Castration-Resistant Prostate Cancer, Ovarian Cancer **Label as of:** 2022-12-21 **Variant class:** BRCA1 mutation

**Indications and usage:**

RUBRACA® is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

Ovarian cancer

- for the maintenance treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)- associated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

Prostate cancer

- for the treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for RUBRACA®.

This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/209115s013lbl.pdf

## Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

NCCN information is current as of 2023-06-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

Some variant specific evidence in this report may be associated with a broader set of alterations from the NCCN Guidelines. Specific variants listed in this report were sourced from approved therapies or scientific literature. These therapeutic options are appropriate for certain population segments with cancer. Refer to the NCCN Guidelines® for full recommendation.

## BRCA1 p.(C328*) c.981_982delAT

### ● bevacizumab + olaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### ● niraparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Persistent, Recurrent, Partial response, Complete response (Maintenance therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### ● niraparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### ● olaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Persistent, Recurrent, Partial response, Complete response (Maintenance therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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## BRCA1 p.(C328*) c.981_982delAT (continued)

### olaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### rucaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Persistent, Recurrent, Partial response, Complete response (Maintenance therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### niraparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### olaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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## BRCA1 p.(C328*) c.981_982delAT (continued)

### rucaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### niraparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 3

**Population segment (Line of therapy):**
- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Other recommended intervention

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### rucaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 3

**Population segment (Line of therapy):**
- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Other recommended intervention

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

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### olaparib

**Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Adenocarcinoma; Non Visceral Metastasis, Visceral Metastases (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Prostate Cancer [Version 1.2023]

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### rucaparib

**Cancer type:** Pancreatic Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Adenocarcinoma; Metastatic (Maintenance therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 1.2023]

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## BRCA1 p.(C328*) c.981_982delAT (continued)

### rucaparib

**Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Adenocarcinoma; Non Visceral Metastasis, Visceral Metastases (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Prostate Cancer [Version 1.2023]

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### olaparib

**Cancer type:** Breast Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**
- Stage IV; Invasive (Line of therapy not specified); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Breast Cancer [Version 4.2023]

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### olaparib

**Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**
- Adenocarcinoma; Visceral Metastases (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Prostate Cancer [Version 1.2023]

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### rucaparib

**Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 mutation

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**
- Adenocarcinoma; Visceral Metastases (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Prostate Cancer [Version 1.2023]

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## Current EMA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

EMA information is current as of 2023-06-14. For the most up-to-date information, search www.ema.europa.eu/ema.

## BRCA1 p.(C328*) c.981_982delAT

### ◑ olaparib, bevacizumab + olaparib

**Cancer type:** Castration-Resistant Prostate Cancer, Ovarian Cancer

**Label as of:** 2023-05-04

**Variant class:** BRCA1 mutation

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/lynparza-epar-product-information_en.pdf

### ○ abiraterone + niraparib

**Cancer type:** Castration-Resistant Prostate Cancer

**Label as of:** 2023-06-02

**Variant class:** BRCA1 mutation

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/akeega-epar-product-information_en.pdf

## Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

ESMO information is current as of 2023-06-01. For the most up-to-date information, search www.esmo.org.

## BRCA1 p.(C328*) c.981_982delAT

### ● bevacizumab + olaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA mutation or HR Deficient

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Epithelial; Relapsed (Maintenance therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 19 July 2021, 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

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### ● niraparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA mutation or HR Deficient

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Epithelial; Relapsed (Maintenance therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 19 July 2021, 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

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### ● olaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Epithelial; Relapsed (Maintenance therapy); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 19 July 2021, 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

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### ● rucaparib

**Cancer type:** Ovarian Cancer **Variant class:** BRCA mutation

**ESMO Level of Evidence/Grade of Recommendation:** III / A

**Population segment (Line of therapy):**
- Epithelial; Recurrent (Line of therapy not specified)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 19 July 2021, 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

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## BRCA1 p.(C328*) c.981_982delAT (continued)

### olaparib

**Cancer type:** Breast Cancer **Variant class:** BRCA1 mutation

**Other criteria:** ERBB2 negative, ER positive

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Luminal A; Advanced, Metastatic (Second-line therapy); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021) VOLUME 32, ISSUE 12, P1475-1495, DECEMBER 01, 2021; DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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### talazoparib

**Cancer type:** Breast Cancer **Variant class:** BRCA1 mutation

**Other criteria:** ERBB2 negative, ER positive

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Luminal A; Advanced, Metastatic (Second-line therapy); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021) VOLUME 32, ISSUE 12, P1475-1495, DECEMBER 01, 2021; DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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### olaparib

**Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / B

**Population segment (Line of therapy):**
- Metastatic, Progression (Line of therapy not specified); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Cancer of the Prostate [Ann Oncol (2020) (eUpdate 21 March 2023)]

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### olaparib

**Cancer type:** Biliary Tract Carcinoma **Variant class:** BRCA1 mutation

**ESMO Level of Evidence/Grade of Recommendation:** V / B

**Population segment (Line of therapy):**
- (Second-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Biliary Cancer [Ann Oncol (2023), doi: https://doi.org/10.1016/j.annonc.2022.10.506]

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# Alerts Informed By Public Data Sources

## Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2023-06-14. For the most up-to-date information, search www.fda.gov.

## BRCA1 p.(C328*) c.981_982delAT

### pidnarulex

**Cancer type:** Breast Cancer, Ovarian Cancer

**Variant class:** HR Deficient

**Supporting Statement:**
The FDA has granted Fast Track Designation to the small molecule inhibitor, pidnarulex for BRCA1/2, PALB2, or other HRD mutations in breast and ovarian cancers.

**Reference:**

https://www.senhwabio.com//en/news/20220125

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