Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
No.201, Sec. 2, Shipai Rd., Beitou District, Taipei City, Taiwan
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Sample Information

Patient Name: 郭樹鳳
Gender: Female
ID No.: A223575147
History No.: 25102641
Age: 60

Ordering Doctor: DOC3577C 黃楷中
Ordering REQ.: 0CWGBDM
Signing in Date: 2024/1/22

Path No.: M113-00025
MP No.: BR24008
Assay: Oncomine BRCA1/2 Assay
Sample Type: FFPE
Block No.: S113-02909D
Percentage of tumor cells: 70%

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

Note:

Sample Cancer Type: Ovarian Cancer

Report Highlights

1 Relevant Biomarkers
8 Therapies Available
0 Clinical Trials

Relevant Ovarian Cancer Variants

Gene	Finding
BRCA1	None detected
BRCA2	***BRCA2 p.(A938Pfs*21) c.2808_2811delACAA***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*BRCA2 p.(A938Pfs*21) c.2808_2811delACAA* BRCA2 DNA repair associated Allele Frequency: 72.81%	**bevacizumab + olaparib** [1, 2] **olaparib** [1, 2] **rucaparib** [1] niraparib	**abiraterone + niraparib** [1, 2] **bevacizumab + olaparib** [1, 2] **olaparib** [1, 2] **rucaparib** [1] **talazoparib + hormone therapy** [1] niraparib	0

Public data sources included in relevant therapies: FDA1, NCCN, **EMA**2, ESMO

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2024.01(006). The content of this report has not been evaluated or approved by FDA, EMA or other regulatory agencies.

Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
			olaparib + hormone therapy talazoparib	

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
BRCA2	p.(A938Pfs*21)	c.2808_2811delACAA	chr13:32911297	72.81%	NM_000059.3	frameshift Deletion	Pathogenic	1964
BRCA2	p.(?)	c.-26G>A	chr13:32890572	29.30%	NM_000059.3	unknown	Benign	2000
BRCA2	p.(N372H)	c.1114A>C	chr13:32906729	72.51%	NM_000059.3	missense	Benign	1997
BRCA2	p.(K1132=)	c.3396A>G	chr13:32911888	26.95%	NM_000059.3	synonymous	Benign	2000
BRCA2	p.(L1521=)	c.4563A>G	chr13:32913055	99.85%	NM_000059.3	synonymous	Benign	1996
BRCA2	p.(V2171=)	c.6513G>C	chr13:32915005	100.00%	NM_000059.3	synonymous	Benign	2000
BRCA2	p.(S2414=)	c.7242A>G	chr13:32929232	25.20%	NM_000059.3	synonymous	Benign	2000
BRCA2	p.(V2466A)	c.7397T>C	chr13:32929387	99.75%	NM_000059.3	missense	Benign	1998

[1] Based on Clinvar version 20200329

Biomarker Descriptions

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA

BRCA2 DNA repair associated

Background: Homologous recombination repair (HRR) is a DNA repair mechanism that targets double stranded breaks (DSBs) and interstrand cross-links (ICL) in DNA[1]. Homologous recombination deficiency (HRD) is characterized by the cell's inability to repair these DSBs[1,2]. 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[3,4,5,6]. A consequence of HRD due to the failure to repair DSBs is genomic instability[7,8]. Genomic instability is an increased tendency towards acquiring genomic alterations during cell division[9,10,11,12,13,14]. 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)[10,15,16]. Variations of genomic instability include chromosomal instability, intrachromosomal instability, microsatellite instability, and epigenetic instability[9]. 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[17,18,19]. For this reason, the alterations characteristic of genomic instability are referred to as genomic scars[20,21]. 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)[1,22]. Current methods for HRD detection are heterogeneous and the definition for HRD positive tumors varies depending on the cancer type[1]. 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)[1,7,23,24].

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[25]. 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

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Biomarker Descriptions (continued)

cell carcinoma[25]. 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[26,27,28,29,30,31,32,33]. 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[34,35]. 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[34,35].

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[36,37,38]. 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[1,39,40,41]. Several PARP inhibitors are approved by the FDA for various cancers associated with markers of HRD. Olaparib[42] 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[42]. 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[4,42,43]. Olaparib is also approved for gBRCAm HER2 negative breast cancer and as maintenance therapies for gBRCAm pancreatic cancers[42]. Other PARP inhibitors that are FDA approved for BRCA mutated cancers include rucaparib[44] (2016) that is indicated for gBRCAm or sBRCAm ovarian and prostate cancers, niraparib[45] (2017) that is indicated for gBRCAm ovarian cancer, and talazoparib[46] (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[47]. In addition to PARP inhibitors, other drugs which promote synthetic lethality have been investigated for BRCA1/2 mutations. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[48], for BRCA1/2, PALB2, or other HRR gene mutations in breast and ovarian cancers. Like PARP inhibitors, pidnarulex[48] 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[49]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[50]. 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[50,51,52,53].

Relevant Therapy Summary

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

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
olaparib	◑	◑	◑	◑	✖
rucaparib	◑	◑	✖	●	✖
bevacizumab + olaparib	◑	●	◑	●	✖
abiraterone + niraparib	○	○	○	✖	✖
talazoparib + enzalutamide	○	○	✖	✖	✖
niraparib	✖	◑	✖	●	✖
olaparib + abiraterone acetate	✖	○	✖	✖	✖
talazoparib	✖	✖	✖	○	✖

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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 2023-12-13. For the most up-to-date information, search www.fda.gov.

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA

◑ olaparib, bevacizumab + olaparib

Cancer type: Castration-Resistant Prostate Cancer, Ovarian Cancer **Label as of:** 2023-11-06 **Variant class:** BRCA2 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 deleterious or suspected deleterious germline or somatic BRCA-mutated recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

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/2023/208558s028lbl.pdf

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BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

rucaparib

Cancer type: Castration-Resistant Prostate Cancer, Ovarian Cancer **Label as of:** 2022-12-21 **Variant class:** BRCA2 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

abiraterone + niraparib

Cancer type: Castration-Resistant Prostate Cancer **Label as of:** 2023-08-11 **Variant class:** BRCA2 mutation

Indications and usage:
AKEEGA® is a combination of niraparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, and abiraterone acetate, a CYP17 inhibitor indicated with prednisone 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 test for AKEEGA®.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216793s000lbl.pdf

talazoparib + enzalutamide

Cancer type: Castration-Resistant Prostate Cancer **Label as of:** 2023-06-20 **Variant class:** BRCA2 mutation

Indications and usage:

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

Breast Cancer

- As a single agent, for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for TALZENNA®.

HRR Gene-mutated mCRPC

- In combination with enzalutamide for the treatment of adult patients with HRR gene-mutated metastatic castration-resistant prostate cancer (mCRPC).

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/211651s010lbl.pdf

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2024.01(006).

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 2023-12-01. To view the most recent and complete version of the guideline, go online to 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.

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BRCA2 p.(A938Pfs*21) c.2808_2811delACAA

● bevacizumab + olaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 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 2.2023]

● niraparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 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 2.2023]

● olaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 2.2023]

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

olaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 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 2.2023]

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rucaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 2.2023]

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niraparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 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 2.2023]

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olaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 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 2.2023]

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BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

rucaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 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 2.2023]

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niraparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 3

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

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 2.2023]

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rucaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 3

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

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 2.2023]

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abiraterone + niraparib

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma; Non Visceral Metastasis, Visceral Metastases (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 4.2023]

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BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

olaparib

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 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 4.2023]

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olaparib + abiraterone acetate

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma; Non Visceral Metastasis, Visceral Metastases (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 4.2023]

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talazoparib + enzalutamide

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma; Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 4.2023]

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abiraterone + niraparib

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 4.2023]

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niraparib

Cancer type: Uterine Leiomyosarcoma **Variant class:** BRCA2 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2024]

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BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

olaparib

Cancer type: Uterine Leiomyosarcoma **Variant class:** BRCA2 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2024]

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olaparib + abiraterone acetate

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 4.2023]

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rucaparib

Cancer type: Pancreatic Cancer **Variant class:** BRCA2 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 2.2023]

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rucaparib

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 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 4.2023]

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rucaparib

Cancer type: Uterine Leiomyosarcoma **Variant class:** BRCA2 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2024]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2024.01(006).

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

talazoparib + enzalutamide

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 4.2023]

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abiraterone + niraparib

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 4.2023]

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olaparib

Cancer type: Breast Cancer **Variant class:** BRCA2 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:** BRCA2 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 4.2023]

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rucaparib

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 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 4.2023]

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BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

talazoparib + enzalutamide

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 4.2023]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2024.01(006).

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 2023-12-13. For the most up-to-date information, search www.ema.europa.eu/ema.

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA

◑ olaparib, bevacizumab + olaparib

Cancer type: Castration-Resistant Prostate Cancer, Ovarian Cancer

Label as of: 2023-09-21

Variant class: BRCA2 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: BRCA2 mutation

Reference:

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2024.01(006).

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 2023-12-01. For the most up-to-date information, search www.esmo.org.

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA

● bevacizumab + olaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation or HR Deficient

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2023; Volume 34 issue 10 pp:833-848 https://doi.org/10.1016/j.annonc.2023.07.011(Published)]

● niraparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation or HR Deficient

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2023; Volume 34 issue 10 pp:833-848 https://doi.org/10.1016/j.annonc.2023.07.011(Published)]

● niraparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2023; Volume 34 issue 10 pp:833-848 https://doi.org/10.1016/j.annonc.2023.07.011(Published)]

● olaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation

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

Population segment (Line of therapy):
- Epithelial; Recurrent (Maintenance therapy); ESMO-MCBS v1.1 score: 2
- Epithelial (Maintenance therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2023; Volume 34 issue 10 pp:833-848 https://doi.org/10.1016/j.annonc.2023.07.011(Published)]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2024.01(006).

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

● rucaparib

Cancer type: Ovarian Cancer **Variant class:** BRCA2 mutation

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2023; Volume 34 issue 10 pp:833-848 https://doi.org/10.1016/j.annonc.2023.07.011(Published)]

○ olaparib

Cancer type: Breast Cancer **Variant class:** BRCA2 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]

○ talazoparib

Cancer type: Breast Cancer **Variant class:** BRCA2 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]

○ olaparib

Cancer type: Castration-Resistant Prostate Cancer **Variant class:** BRCA2 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: 3

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2024.01(006).

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA (continued)

olaparib

Cancer type: Biliary Tract Carcinoma **Variant class:** BRCA2 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]

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2023-12-13. For the most up-to-date information, search www.fda.gov.

BRCA2 p.(A938Pfs*21) c.2808_2811delACAA

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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