Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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Sample Information

Patient Name: 張華良
Gender: Male
ID No.: A110319866
History No.: 46709482
Age: 67

Ordering Doctor: DOC2169J 張延驊
Ordering REQ.: G2FCG42
Signing in Date: 2024/1/16

Path No.: M113-00014
MP No.: BR24004
Assay: Oncomine BRCA1/2 Assay
Sample Type: FFPE
Block No.: S110-70271B
Percentage of tumor cells: 60%

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

Note:

Sample Cancer Type: Prostate Adenocarcinoma

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Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*BRCA2 p.(P2802Lfs*19) c.8403delT* BRCA2 DNA repair associated Allele Frequency: 75.61%	None	**abiraterone + niraparib** [1, 2] **bevacizumab + olaparib** [1, 2] **olaparib** [1, 2] **rucaparib** [1] **talazoparib + hormone therapy** [1] niraparib olaparib + hormone therapy talazoparib	1

Public data sources included in relevant therapies: FDA1, 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.(P2802Lfs*19)	c.8403delT	chr13:32944606	75.61%	NM_000059.3	frameshift Deletion	Pathogenic	1980
BRCA2	p.(?)	c.-26G>A	chr13:32890572	86.78%	NM_000059.3	unknown	Benign	1997
BRCA2	p.(N372H)	c.1114A>C	chr13:32906729	11.55%	NM_000059.3	missense	Benign	2000
BRCA2	p.(K1132=)	c.3396A>G	chr13:32911888	87.94%	NM_000059.3	synonymous	Benign	1999
BRCA2	p.(L1521=)	c.4563A>G	chr13:32913055	99.70%	NM_000059.3	synonymous	Benign	1999
BRCA2	p.(V2171=)	c.6513G>C	chr13:32915005	100.00%	NM_000059.3	synonymous	Benign	1991
BRCA2	p.(S2414=)	c.7242A>G	chr13:32929232	87.59%	NM_000059.3	synonymous	Benign	1998
BRCA2	p.(V2466A)	c.7397T>C	chr13:32929387	99.60%	NM_000059.3	missense	Benign	1999
BRCA1	p.(S1613G)	c.4837A>G	chr17:41223094	99.80%	NM_007294.4	missense	Benign	2000
BRCA1	p.(S1436=)	c.4308T>C	chr17:41234470	99.60%	NM_007294.4	synonymous	Benign	2000
BRCA1	p.(K1183R)	c.3548A>G	chr17:41244000	99.55%	NM_007294.4	missense	Benign	2000
BRCA1	p.(E1038G)	c.3113A>G	chr17:41244435	98.95%	NM_007294.4	missense	Benign	1999
BRCA1	p.(P871L)	c.2612C>T	chr17:41244936	99.50%	NM_007294.4	missense	Benign	1999
BRCA1	p.(L771=)	c.2311T>C	chr17:41245237	99.30%	NM_007294.4	synonymous	Benign	1999
BRCA1	p.(S694=)	c.2082C>T	chr17:41245466	99.70%	NM_007294.4	synonymous	Benign	1996

[1] Based on Clinvar version 20200329

Biomarker Descriptions

BRCA2 p.(P2802Lfs*19) c.8403delT

BRCA2 DNA repair associated

Background: The breast cancer early onset gene 2 (BRCA2) 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 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, the cumulative risk of breast cancer by 80 years of age was 69-72% and the cumulative risk of ovarian cancer by 70 years was 20-48%[3,6].

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 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: 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

Biomarker Descriptions (continued)

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 BRCA2. Rucaparib[21] is also approved (2020) for deleterious gBRCAm or sBRCAm mCRPC and ovarian cancer. Talazoparib[22] (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Additionally, talazoparib[22] in combination with enzalutamide is approved (2023) for metastatic castration-resistant prostate cancer (mCRPC) with mutations in HRR genes that includes BRCA2. Niraparib[23] (2017) is another PARPi approved for the treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancers with a deleterious or suspected deleterious BRCA mutation. Niraparib in combination with abiraterone acetate[24] received FDA approval (2023) for the treatment of deleterious or suspected deleterious BRCA-mutated (BRCAm) mCRPC. Despite tolerability and efficacy, acquired resistance to PARP inhibition has been clinically reported[25]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[26]. 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[27], 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.

Relevant Therapy Summary

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

BRCA2 p.(P2802Lfs*19) c.8403delT

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bevacizumab + olaparib	○	○	○	○	✖
olaparib	○	○	○	○	✖
abiraterone + niraparib	○	○	○	✖	✖
rucaparib	○	○	✖	○	✖
talazoparib + enzalutamide	○	○	✖	✖	✖
niraparib	✖	○	✖	○	✖
olaparib + abiraterone acetate	✖	○	✖	✖	✖
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 2023-11-15. For the most up-to-date information, search www.fda.gov.

BRCA2 p.(P2802Lfs*19) c.8403delT

○ 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

BRCA2 p.(P2802Lfs*19) c.8403delT (continued)

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

BRCA2 p.(P2802Lfs*19) c.8403delT (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

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

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 2023-11-01. 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.

BRCA2 p.(P2802Lfs*19) c.8403delT

○ 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]

○ 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; Recurrent, Partial response, Complete response (Maintenance therapy); Useful in certain circumstances

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

BRCA2 p.(P2802Lfs*19) c.8403delT (continued)

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]

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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]

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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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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]

BRCA2 p.(P2802Lfs*19) c.8403delT (continued)

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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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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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: 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]

BRCA2 p.(P2802Lfs*19) c.8403delT (continued)

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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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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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: 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]

BRCA2 p.(P2802Lfs*19) c.8403delT (continued)

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]

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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]

BRCA2 p.(P2802Lfs*19) c.8403delT (continued)

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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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]

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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]

BRCA2 p.(P2802Lfs*19) c.8403delT (continued)

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]

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 2023-11-15. For the most up-to-date information, search www.ema.europa.eu/ema.

BRCA2 p.(P2802Lfs*19) c.8403delT

○ 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

○ 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

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 2023-11-01. For the most up-to-date information, search www.esmo.org.

BRCA2 p.(P2802Lfs*19) c.8403delT

○ bevacizumab + olaparib

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

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 (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: 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]

BRCA2 p.(P2802Lfs*19) c.8403delT (continued)

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)]

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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)]

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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]

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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]

BRCA2 p.(P2802Lfs*19) c.8403delT (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]

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