



Sample Information

Patient Name: 洪薇鈞
Gender: Female
ID No.: R222964055
History No.: 41123324
Age: 34

Ordering Doctor: DOC2589K 曾令民
Ordering REQ.: D6NAKM8
Signing in Date: 2022/03/31

Path No.: S111-98887
MP No.: BR22026
Assay: Oncomine BRCA Assay
Sample Type: Blood
Date of blood drawing: 2022/03/24

Reporting Doctor: DOC5452C 周德盈 (Phone: 8#5452)

Note:

Sample Cancer Type: Breast Cancer

| Table of Contents | Page | Report Highlights |
|--------------------------|------|-----------------------|
| Variant Details | 2 | 1 Relevant Biomarkers |
| Biomarker Descriptions | 2 | 5 Therapies Available |
| Relevant Therapy Summary | 3 | 0 Clinical Trials |
| Relevant Therapy Details | 4 | |
| Alert Details | 14 | |

Relevant Biomarkers

| Genomic Alteration | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|---|---|--|-----------------|
| BRCA2 p.(E1308*) c.3922G>T BRCA2 DNA repair associated Allele Frequency: 49.71% Prognostic significance: None Diagnostic significance: None | olaparib talazoparib | bevacizumab + olaparib ^{1,2} niraparib ¹ olaparib ^{1,2} rucaparib ^{1,2} | 0 |

Public data sources included in relevant therapies: FDA¹, NCCN, EMA², ESMO
Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

Variant Details

DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Locus | Allele Frequency | Transcript | Variant Effect | ClinVar ¹ | Coverage |
|-------|-------------------|-----------|----------------|------------------|-------------|----------------|------------------------|----------|
| BRCA2 | p.(E1308*) | c.3922G>T | chr13:32912414 | 49.71% | NM_000059.3 | nonsense | Pathogenic | 1400 |
| BRCA2 | p.(N289H) | c.865A>C | chr13:32906480 | 46.78% | NM_000059.3 | missense | Benign | 1445 |
| BRCA2 | p.(N372H) | c.1114A>C | chr13:32906729 | 49.40% | NM_000059.3 | missense | Benign | 1996 |
| BRCA2 | p.(S455=) | c.1365A>G | chr13:32906980 | 47.50% | NM_000059.3 | synonymous | Benign | 1998 |
| BRCA2 | p.(H743=) | c.2229T>C | chr13:32910721 | 51.55% | NM_000059.3 | synonymous | Benign | 2000 |
| BRCA2 | p.(N991D) | c.2971A>G | chr13:32911463 | 51.72% | NM_000059.3 | missense | Benign | 1334 |
| BRCA2 | p.(L1521=) | c.4563A>G | chr13:32913055 | 99.86% | NM_000059.3 | synonymous | Benign | 1397 |
| BRCA2 | p.(V2171=) | c.6513G>C | chr13:32915005 | 100.00% | NM_000059.3 | synonymous | Benign | 2000 |
| BRCA2 | p.(V2466A) | c.7397T>C | chr13:32929387 | 99.89% | NM_000059.3 | missense | Benign | 1817 |
| BRCA1 | p.(S1613G) | c.4837A>G | chr17:41223094 | 99.85% | NM_007294.4 | missense | Benign | 2000 |
| BRCA1 | p.(S1436=) | c.4308T>C | chr17:41234470 | 99.80% | NM_007294.4 | synonymous | Benign | 1999 |
| BRCA1 | p.(S1217P) | c.3649T>C | chr17:41243899 | 50.95% | NM_007294.4 | missense | Uncertain significance | 1998 |
| BRCA1 | p.(K1183R) | c.3548A>G | chr17:41244000 | 99.65% | NM_007294.4 | missense | Benign | 1999 |
| BRCA1 | p.(E1038G) | c.3113A>G | chr17:41244435 | 99.55% | NM_007294.4 | missense | Benign | 1999 |
| BRCA1 | p.(P871L) | c.2612C>T | chr17:41244936 | 99.70% | NM_007294.4 | missense | Benign | 2000 |
| BRCA1 | p.(L771=) | c.2311T>C | chr17:41245237 | 99.90% | NM_007294.4 | synonymous | Benign | 1999 |
| BRCA1 | p.(S694=) | c.2082C>T | chr17:41245466 | 99.80% | NM_007294.4 | synonymous | Benign | 1999 |

¹ Based on Clinvar version 20200329

Biomarker Descriptions

BRCA2 (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. 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 cancer³ and in men for breast and prostate cancer^{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 cancer⁶.

Alterations and prevalence: Inherited BRCA1/2 mutations occur in 1:400 to 1:500 individuals and are observed in 10-15% of ovarian cancer and 5-10% of breast cancer^{7,8,9,10,11,12,13}. Somatic alterations in BRCA2 are observed in 5-15% of melanomas, uterine, cervical, gastric, colorectal, esophageal, and lung cancers^{14,15}.

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)¹⁶. Inhibitors targeting PARP induce synthetic lethality in recombination deficient BRCA1/2 mutant cells^{17,18}. Consequently, several PARP inhibitors have been FDA approved for BRCA1/2-mutated cancers. Olaparib¹⁹ (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

Biomarker Descriptions (continued)

gBRCAm HER2-negative metastatic breast cancer and metastatic pancreatic adenocarcinoma. Additionally, olaparib¹⁹ 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. Rucaparib²⁰ (2016) was the first PARPi approved for the treatment of patients with either gBRCAm or sBRCAm epithelial ovarian, fallopian tube, or primary peritoneal cancers and is also approved (2020) for deleterious gBRCAm or sBRCAm mCRPC. Talazoparib²¹ (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Niraparib²² (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. Despite tolerability and efficacy, acquired resistance to PARP inhibition has been clinically reported²³. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality²⁴. 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, pidnarulex²⁵, 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.(E1308*) c.3922G>T

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|------------------------|-------------------------------------|-------------------------------------|-------------------------------------|----------------------------------|-------------------------------------|
| olaparib | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input checked="" type="radio"/> | <input checked="" type="checkbox"/> |
| bevacizumab + olaparib | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input checked="" type="checkbox"/> |
| rucaparib | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input checked="" type="checkbox"/> |
| niraparib | <input type="radio"/> | <input type="radio"/> | <input checked="" type="checkbox"/> | <input type="radio"/> | <input checked="" type="checkbox"/> |
| talazoparib | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="radio"/> | <input checked="" type="checkbox"/> |

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 2022-02-16. For the most up-to-date information, search www.fda.gov.

BRCA2 p.(E1308*) c.3922G>T

☐ niraparib

Cancer type: Ovarian Cancer

Label as of: 2021-07-27

Variant class: BRCA2 mutation or HR Deficient

Indications and usage:

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

- for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.
- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
- for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 3 or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either:
 - a deleterious or suspected deleterious BRCA mutation, or
 - genomic instability and who have progressed more than 6 months after response to the last platinum-based chemotherapy.

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208447s022s024lbl.pdf

BRCA2 p.(E1308*) c.3922G>T (continued)

○ olaparib, bevacizumab + olaparib

Cancer type: Castration-Resistant Prostate Cancer, Ovarian Cancer

Label as of: 2022-01-31

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 recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.
- for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

Breast cancer

- 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®.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208558s021lbl.pdf

BRCA2 p.(E1308*) c.3922G>T (continued)**○ rucaparib**

Cancer type: Castration-Resistant Prostate Cancer, Ovarian Cancer

Label as of: 2021-09-30

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 recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
- for the treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies. Select patients for therapy based on an FDA-approved companion diagnostic for RUBRACA®.

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/2021/209115s009lbl.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 2022-02-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

BRCA2 p.(E1308*) c.3922G>T

☐ 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 1.2022]

☐ niraparib

Cancer type: Ovarian Cancer

Variant class: BRCA2 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 1.2022]

☐ 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 1.2022]

☐ olaparib

Cancer type: Ovarian Cancer

Variant class: BRCA2 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 1.2022]

BRCA2 p.(E1308*) c.3922G>T (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 1.2022]**○ olaparib****Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA2 mutation**NCCN Recommendation category:** 1**Population segment (Line of therapy):**

- Adenocarcinoma; Metastatic (Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 3.2022]**○ rucaparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA2 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 1.2022]**○ 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 1.2022]

BRCA2 p.(E1308*) c.3922G>T (continued)**○ niraparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA2 mutation or HR Deficient**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2022]**○ niraparib****Cancer type:** Uterine Leiomyosarcoma**Variant class:** BRCA2 mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- (Second-line therapy); Useful in certain circumstances, Consider

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]**○ 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 1.2022]**○ olaparib****Cancer type:** Uterine Leiomyosarcoma**Variant class:** BRCA2 mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- (Second-line therapy); Useful in certain circumstances, Consider

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]

BRCA2 p.(E1308*) c.3922G>T (continued)**○ rucaparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA2 mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2022]**○ rucaparib****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 3.2022]**○ rucaparib****Cancer type:** Uterine Leiomyosarcoma**Variant class:** BRCA2 mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- (Second-line therapy); Useful in certain circumstances, Consider

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]**○ 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 3.2022]**○ 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 3.2022]

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 2022-02-16. For the most up-to-date information, search www.ema.europa.eu/ema.

BRCA2 p.(E1308*) c.3922G>T

☐ olaparib, bevacizumab + olaparib

Cancer type: Castration-Resistant Prostate Cancer, Ovarian Cancer

Label as of: 2022-01-17

Variant class: BRCA2 mutation

Reference:

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

☐ rucaparib

Cancer type: Ovarian Cancer

Label as of: 2021-09-20

Variant class: BRCA2 mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/rubraca-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 2022-02-01. For the most up-to-date information, search www.esmo.org.

BRCA2 p.(E1308*) c.3922G>T

☒ 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)

Reference: ESMO Clinical Practice Guidelines - ESMO-Cancer of the Prostate [Ann Oncol (2020)]

☐ 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)]

BRCA2 p.(E1308*) c.3922G>T (continued)**○ 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)]

○ 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)]


○ 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)]

Alerts Informed By Public Data Sources

Current FDA Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

FDA information is current as of 2022-02-16. For the most up-to-date information, search www.fda.gov.

BRCA2 p.(E1308*) c.3922G>T

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>

Current NCCN Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

NCCN information is current as of 2022-02-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

BRCA2 p.(E1308*) c.3922G>T

bevacizumab

Cancer type: Ovarian Cancer

Variant class: BRCA2 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "bevacizumab monotherapy is no longer recommended for patients with BRCA1/2 mutations"

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2022]

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

References

1. Liu et al. Distinct functions of BRCA1 and BRCA2 in double-strand break repair. *Breast Cancer Res.* 2002;4(1):9-13. PMID: 11879553
2. Jasin. Homologous repair of DNA damage and tumorigenesis: the BRCA connection. *Oncogene.* 2002 Dec 16;21(58):8981-93. PMID: 12483514
3. Kuchenbaecker et al. Risks of Breast, Ovarian, and Contralateral Breast Cancer for BRCA1 and BRCA2 Mutation Carriers. *JAMA.* 2017 Jun 20;317(23):2402-2416. PMID: 28632866
4. Tai et al. Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. *J. Natl. Cancer Inst.* 2007 Dec 5;99(23):1811-4. PMID: 18042939
5. Levy-Lahad et al. Cancer risks among BRCA1 and BRCA2 mutation carriers. *Br. J. Cancer.* 2007 Jan 15;96(1):11-5. PMID: 17213823
6. NCCN Guidelines® - NCCN-Genetic/Familial High-Risk Assessment: Breast and Ovarian [Version 1.2018]. NCCN-Genetic/Familial High-Risk Assessment: Breast and Ovarian
7. ARUP Laboratories University of Utah Department of Pathology.. <https://arupconsult.com/ati/hereditary-breast-and-ovarian-cancer>
8. Petrucelli et al. BRCA1- and BRCA2-Associated Hereditary Breast and Ovarian Cancer. *GeneReviews®* [Internet]. PMID: 20301425
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