



Sample Information

Patient Name: 羅彩嬌
Gender: Female
ID No.: H201549542
History No.: 28227716
Age: 69

Ordering Doctor: DOC1888K 趙大中
Ordering REQ.: D743DFB
Signing in Date: 2023/01/18

Path No.: M112-00013
MP No.: BR23004
Assay: Oncomine BRCA1/2 Assay
Sample Type: Blood
Date of blood drawing: 2023/01/10

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

Note:

Sample Cancer Type: Breast Cancer

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Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	BRCA1 p.(F1734Lfs*31) c.5202delT BRCA1 DNA repair associated Allele Frequency: 51.67%	olaparib talazoparib	bevacizumab + olaparib ^{1,2} olaparib ^{1,2} rucaparib ¹ niraparib	0

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Locus	Allele Frequency	Transcript	Variant Effect	ClinVar ¹	Coverage
BRCA1	p.(F1734Lfs*31)	c.5202delT	chr17:41209143	51.67%	NM_007294.4	frameshift Deletion	Pathogenic	1885
BRCA2	p.(?)	c.-26G>A	chr13:32890572	52.06%	NM_000059.3	unknown	Benign	3004
BRCA2	p.(N372H)	c.1114A>C	chr13:32906729	50.71%	NM_000059.3	missense	Benign	1972
BRCA2	p.(K1132=)	c.3396A>G	chr13:32911888	50.72%	NM_000059.3	synonymous	Benign	3279
BRCA2	p.(L1521=)	c.4563A>G	chr13:32913055	99.82%	NM_000059.3	synonymous	Benign	1099
BRCA2	p.(V2171=)	c.6513G>C	chr13:32915005	99.96%	NM_000059.3	synonymous	Benign	2752
BRCA2	p.(S2414=)	c.7242A>G	chr13:32929232	49.71%	NM_000059.3	synonymous	Benign	1869
BRCA2	p.(V2466A)	c.7397T>C	chr13:32929387	99.71%	NM_000059.3	missense	Benign	1403
BRCA1	p.(S1613G)	c.4837A>G	chr17:41223094	50.55%	NM_007294.4	missense	Benign	3563
BRCA1	p.(S1436=)	c.4308T>C	chr17:41234470	48.72%	NM_007294.4	synonymous	Benign	1560
BRCA1	p.(K1183R)	c.3548A>G	chr17:41244000	49.91%	NM_007294.4	missense	Benign	3999
BRCA1	p.(E1038G)	c.3113A>G	chr17:41244435	50.63%	NM_007294.4	missense	Benign	3194
BRCA1	p.(P871L)	c.2612C>T	chr17:41244936	48.54%	NM_007294.4	missense	Benign	3997
BRCA1	p.(L771=)	c.2311T>C	chr17:41245237	49.84%	NM_007294.4	synonymous	Benign	1234
BRCA1	p.(S694=)	c.2082C>T	chr17:41245466	49.77%	NM_007294.4	synonymous	Benign	3998
BRCA1	p.(K38=)	c.114G>A	chr17:41267763	48.72%	NM_007294.4	synonymous	Benign	2847

¹ Based on Clinvar version 20200329

Biomarker Descriptions

BRCA1 (BRCA1 DNA repair associated)

Background: The breast cancer early onset gene 1 (BRCA1) encodes one of two BRCA proteins (BRCA1 and BRCA2) initially discovered as major hereditary breast cancer genes. Although structurally unrelated, both BRCA1 and BRCA2 exhibit tumor suppressor function and are integrally involved in the homologous recombination repair (HRR) pathway, a pathway critical in the repair of damaged DNA^{1,2}. Specifically, BRCA1/2 are required for the repair of chromosomal double strand breaks (DSBs) which are highly unstable and compromise genome integrity^{1,2}. Inherited pathogenic mutations in BRCA1/2 are known to confer increased risk in women for breast and ovarian cancer and in men for breast and prostate cancer^{3,4,5}. For individuals diagnosed with inherited pathogenic or likely pathogenic BRCA1/2 variants, estimated lifetime risks range from 41% to 90% for developing breast cancer and 8 to 62% for developing ovarian 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 BRCA1 are observed in 2-8% of breast, ovarian, cervical, uterine, diffuse large B-cell lymphoma (DLBCL), melanoma, gastric, bladder, squamous lung, colorectal, and head and neck 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 gBRCAm HER2-negative metastatic breast cancer and metastatic pancreatic adenocarcinoma. Additionally, olaparib¹⁹ is

Biomarker Descriptions (continued)

approved (2020) for metastatic castration-resistant prostate cancer (mCRPC) with deleterious or suspected deleterious, germline or somatic mutations in HRR genes that includes BRCA1. Rucaparib²⁰ 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

BRCA1 p.(F1734Lfs*31) c.5202delT

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="radio"/>
bevacizumab + olaparib	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
rucaparib	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
niraparib	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
talazoparib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>

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 2022-11-16. For the most up-to-date information, search www.fda.gov.

BRCA1 p.(F1734Lfs*31) c.5202delT

☐ olaparib, bevacizumab + olaparib

Cancer type: Castration-Resistant Prostate Cancer, Ovarian Cancer

Label as of: 2022-10-27

Variant class: BRCA1 mutation

Indications and usage:

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

Ovarian cancer

- for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.
- in combination with bevacizumab for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD)-positive status defined by either:
 - a deleterious or suspected deleterious BRCA mutation, and/or
 - genomic instability.

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

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

Breast cancer

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

Pancreatic cancer

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

Prostate cancer

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208558s024lbl.pdf

BRCA1 p.(F1734Lfs*31) c.5202delT (continued)**○ rucaparib**

Cancer type: Castration-Resistant Prostate Cancer

Label as of: 2022-06-10

Variant class: BRCA1 mutation

Indications and usage:

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

Ovarian cancer

- for the maintenance treatment of adult patients with 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/2022/209115s011lbl.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 2022-11-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

BRCA1 p.(F1734Lfs*31) c.5202delT

☐ bevacizumab + olaparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]

☐ niraparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Epithelial, Fallopian Tube, Primary Peritoneal; Persistent, Recurrent, Partial response, Complete response (Maintenance therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]

☐ niraparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]

☐ olaparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Epithelial, Fallopian Tube, Primary Peritoneal; Persistent, Recurrent, Partial response, Complete response (Maintenance therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]

BRCA1 p.(F1734Lfs*31) c.5202delT (continued)**○ olaparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA1 mutation**NCCN Recommendation category:** 1**Population segment (Line of therapy):**

- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]**○ olaparib****Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 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 1.2023]**○ rucaparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA1 mutation**NCCN Recommendation category:** 1**Population segment (Line of therapy):**

- Epithelial, Fallopian Tube, Primary Peritoneal; Persistent, Recurrent, Partial response, Complete response (Maintenance therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]**○ niraparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA1 mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]

BRCA1 p.(F1734Lfs*31) c.5202delT (continued)**○ olaparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA1 mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Epithelial, Fallopian Tube, Primary Peritoneal; Stage II, Stage III, Stage IV; Partial response, Complete response (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]**○ rucaparib****Cancer type:** Pancreatic Cancer**Variant class:** BRCA1 mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

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

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 1.2022]**○ rucaparib****Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 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 1.2023]**○ olaparib****Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 mutation**NCCN Recommendation category:** 2B**Population segment (Line of therapy):**

- Adenocarcinoma; Visceral Metastases (Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 1.2023]**○ rucaparib****Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** BRCA1 mutation**NCCN Recommendation category:** 2B**Population segment (Line of therapy):**

- Adenocarcinoma; Visceral Metastases (Subsequent therapy); Useful in certain circumstances

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

BRCA1 p.(F1734Lfs*31) c.5202delT (continued)**○ niraparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA1 mutation**NCCN Recommendation category:** 3**Population segment (Line of therapy):**

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

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]**○ rucaparib****Cancer type:** Ovarian Cancer**Variant class:** BRCA1 mutation**NCCN Recommendation category:** 3**Population segment (Line of therapy):**

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

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]

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 2022-11-16. For the most up-to-date information, search www.ema.europa.eu/ema.

BRCA1 p.(F1734Lfs*31) c.5202delT

☐ olaparib, bevacizumab + olaparib

Cancer type: Castration-Resistant Prostate Cancer, Ovarian Cancer

Label as of: 2022-10-03

Variant class: BRCA1 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 2022-11-01. For the most up-to-date information, search www.esmo.org.

BRCA1 p.(F1734Lfs*31) c.5202delT

☒ olaparib

Cancer type: Breast Cancer

Variant class: BRCA1 mutation

Other criteria: ERBB2 negative, ER positive

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

Population segment (Line of therapy):

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

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

☒ talazoparib

Cancer type: Breast Cancer

Variant class: BRCA1 mutation

Other criteria: ERBB2 negative, ER positive

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

Population segment (Line of therapy):

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

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

☐ olaparib

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

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

Population segment (Line of therapy):

- Metastatic, Progression (Line of therapy not specified)

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)]

BRCA1 p.(F1734Lfs*31) c.5202delT (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 2022-11-16. For the most up-to-date information, search www.fda.gov.

BRCA1 p.(F1734Lfs*31) c.5202delT

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 2022-11-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

BRCA1 p.(F1734Lfs*31) c.5202delT

bevacizumab

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 5.2022]

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
9. Pruthi et al. Identification and Management of Women With BRCA Mutations or Hereditary Predisposition for Breast and Ovarian Cancer. *Mayo Clin. Proc.* 2010 Dec;85(12):1111-20. PMID: 21123638
10. Walsh et al. Mutations in 12 genes for inherited ovarian, fallopian tube, and peritoneal carcinoma identified by massively parallel sequencing. *Proc. Natl. Acad. Sci. U.S.A.* 2011 Nov 1;108(44):18032-7. PMID: 22006311
11. Alsop et al. BRCA mutation frequency and patterns of treatment response in BRCA mutation-positive women with ovarian cancer: a report from the Australian Ovarian Cancer Study Group. *J. Clin. Oncol.* 2012 Jul 20;30(21):2654-63. PMID: 22711857
12. Whittemore et al. Prevalence of BRCA1 mutation carriers among U.S. non-Hispanic Whites. *Cancer Epidemiol. Biomarkers Prev.* 2004 Dec;13(12):2078-83. PMID: 15598764
13. Anglian Breast Cancer Study Group. Prevalence and penetrance of BRCA1 and BRCA2 mutations in a population-based series of breast cancer cases. Anglian Breast Cancer Study Group. *Br. J. Cancer.* 2000 Nov;83(10):1301-8. PMID: 11044354
14. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. *Nat. Genet.* 2013 Oct;45(10):1113-20. PMID: 24071849
15. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov.* 2012 May;2(5):401-4. PMID: 22588877
16. Hodgson et al. Candidate biomarkers of PARP inhibitor sensitivity in ovarian cancer beyond the BRCA genes. *Br. J. Cancer.* 2018 Nov;119(11):1401-1409. PMID: 30353044
17. Bryant et al. Specific killing of BRCA2-deficient tumours with inhibitors of poly(ADP-ribose) polymerase. *Nature.* 2005 Apr 14;434(7035):913-7. PMID: 15829966
18. Farmer et al. Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy. *Nature.* 2005 Apr 14;434(7035):917-21. PMID: 15829967
19. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208558s024lbl.pdf
20. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/209115s011lbl.pdf
21. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/211651s008lbl.pdf
22. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208447s026lbl.pdf
23. Barber et al. Secondary mutations in BRCA2 associated with clinical resistance to a PARP inhibitor. *J. Pathol.* 2013 Feb;229(3):422-9. PMID: 23165508
24. D'Andrea. Mechanisms of PARP inhibitor sensitivity and resistance. *DNA Repair (Amst.).* 2018 Nov;71:172-176. PMID: 30177437
25. <https://www.senhwabio.com/en/news/20220125>