Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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Sample Information

Patient Name: 林阿慎
Gender: Female
ID No.: F220384998
History No.: 47601898
Age: 64

Ordering Doctor: DOC3697E 陳怡仁
Ordering REQ.: 0BLQPQY
Signing in Date: 2021/09/29

Path No.: S110-99657
MP No.: BR21041
Assay: Oncomine BRCA1/2 Assay
Sample Type: FFPE
Block No.: S110-26733K
Percentage of tumor cells: 80%

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

Note:

Sample Cancer Type: Ovarian Cancer

Report Highlights

1 Relevant Biomarkers
1 Therapies Available
0 Clinical Trials

Relevant Ovarian Cancer Variants

Gene	Finding
BRCA1	***BRCA1 deletion***
BRCA2	None detected

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*BRCA1 deletion* BRCA1 DNA repair associated	niraparib	None	0

Public data sources included in relevant therapies: FDA1, NCCN, **EMA**2, ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
BRCA2	p.(?)	c.-26G>A	.	chr13:32890572	50.73%	NM_000059.3	unknown	1997
BRCA2	p.(N289H)	c.865A>C	.	chr13:32906480	48.32%	NM_000059.3	missense	1995
BRCA2	p.(S455=)	c.1365A>G	.	chr13:32906980	49.05%	NM_000059.3	synonymous	2000
BRCA2	p.(H743=)	c.2229T>C	.	chr13:32910721	50.88%	NM_000059.3	synonymous	1999
BRCA2	p.(N991D)	c.2971A>G	.	chr13:32911463	51.23%	NM_000059.3	missense	1999
BRCA2	p.(K1132=)	c.3396A>G	.	chr13:32911888	50.78%	NM_000059.3	synonymous	1999
BRCA2	p.(L1521=)	c.4563A>G	.	chr13:32913055	99.95%	NM_000059.3	synonymous	1996
BRCA2	p.(V2171=)	c.6513G>C	.	chr13:32915005	100.00%	NM_000059.3	synonymous	1995
BRCA2	p.(S2414=)	c.7242A>G	.	chr13:32929232	47.95%	NM_000059.3	synonymous	2000
BRCA2	p.(V2466A)	c.7397T>C	.	chr13:32929387	99.75%	NM_000059.3	missense	1997

Copy Number Variations

Gene	Locus	Copy Number
BRCA1	chr17:41197601	1

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. 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[3] 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 cancer[6].

Alterations and prevalence: Inherited BRCA1/2 mutations occur in 1:400 to 1:500 individuals and are observed in 10-15% of ovarian cancer 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. Olaparib[19] (2014) was the first PARPi to be approved by the FDA for BRCA1/2 aberrations. Originally approved for the treatment of germline variants, olaparib is now indicated (2018) for the maintenance treatment of both germline BRCA1/2-mutated (gBRCAm) and somatic BRCA1/2-mutated (sBRCAm) epithelial ovarian, fallopian tube, or primary peritoneal cancers that are responsive to platinum-based chemotherapy. Olaparib is also indicated for the treatment of patients with gBRCAm HER2-negative metastatic breast cancer and metastatic pancreatic adenocarcinoma. Additionally, olaparib[19] is approved (2020) for metastatic castration-resistant prostate cancer (mCRPC) with deleterious or suspected deleterious, germline or somatic mutations in HRR genes that includes BRCA1. Rucaparib[20] (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. Talazoparib[21] (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Niraparib[22] (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

Biomarker Descriptions (continued)

resistance to PARP inhibition has been clinically reported[23]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[24].

Relevant Therapy Summary

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

BRCA1 deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
niraparib	✖	●	✖	✖	✖

Relevant Therapy Details

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 2021-07-01. 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 deletion

● niraparib

Cancer type: Ovarian Cancer **Variant class:** 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 1.2021]

Clinical Trials in Taiwan region:

Signatures

Testing Personnel:

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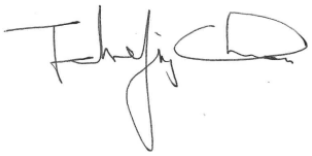
Laboratory Supervisor:

2021.10.01
09:49:00 +08'00'

Pathologist:



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