



Sample Information

Patient Name: 陳美玲

Gender: Female

ID No.: A222556844

History No.: 17086883

Age: 58

Ordering Doctor: DOC3697E 陳怡仁

Ordering REQ.: 0BAJFFF

Signing in Date: 2020/12/30

Path No.: S109-96879

MP No.: BR20008

Assay: Oncomine BRCA1/2 Assay

Sample Type: FFPE

Block No.: S108-68476E

Percentage of tumor cells: 70%

Note:

Sample Cancer Type: Ovarian Cancer

Table of Contents

	Page
Variant Details	2
Biomarker Descriptions	2
Relevant Therapy Summary	3
Relevant Therapy Details	5

Report Highlights

1 Relevant Biomarkers
4 Therapies Available
30 Clinical Trials

Relevant Ovarian Cancer Variants

Gene	Finding
BRCA1	BRCA1 p.(Q1742*) c.5224C>T
BRCA2	Not detected

Relevant Biomarkers

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
BRCA1 p.(Q1742*) c.5224C>T BRCA1, DNA repair associated Allele Fraction: 0.489	bevacizumab + olaparib ¹ niraparib ¹ olaparib ^{1, 2} rucaparib ^{1, 2}	bevacizumab + olaparib ¹ olaparib ¹ rucaparib ¹	30

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



Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Locus	Allele Fraction	Transcript	Variant Effect	ClinVar ¹	Coverage
BRCA1	p.(Q1742*)	c.5224C>T	chr17:41215382	0.489	NM_007300.3	nonsense	Pathogenic	1990
BRCA2	p.(N372H)	c.1114A>C	chr13:32906729	0.345	NM_000059.3	missense	Benign	1997
BRCA2	p.(=)	c.3807T>C	chr13:32912299	0.666	NM_000059.3	synonymous	Benign	1997
BRCA2	p.(=)	c.4563A>G	chr13:32913055	0.998	NM_000059.3	synonymous	Benign	1996
BRCA2	p.(=)	c.6513G>C	chr13:32915005	1.000	NM_000059.3	synonymous	Benign	1995
BRCA2	p.(V2466A)	c.7397T>C	chr13:32929387	0.997	NM_000059.3	missense	Conflicting interpretations of pathogenicity	1998
BRCA1	p.(S1634G)	c.4900A>G	chr17:41223094	0.212	NM_007300.3	missense	Benign	1997
BRCA1	p.(=)	c.4308T>C	chr17:41234470	0.226	NM_007300.3	synonymous	Benign	1998
BRCA1	p.(K1183R)	c.3548A>G	chr17:41244000	0.243	NM_007300.3	missense	Benign	2000
BRCA1	p.(E1038G)	c.3113A>G	chr17:41244435	0.242	NM_007300.3	missense	Benign	1999
BRCA1	p.(P871L)	c.2612C>T	chr17:41244936	0.263	NM_007300.3	missense	Benign	1999
BRCA1	p.(=)	c.2311T>C	chr17:41245237	0.242	NM_007300.3	synonymous	Benign	2000
BRCA1	p.(=)	c.2082C>T	chr17:41245466	0.265	NM_007300.3	synonymous	Benign	1999

¹ Based on Clinvar version 20180225

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 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 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 approved



Biomarker Descriptions (continued)

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

Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ No evidence

BRCA1 p.(Q1742*) c.5224C>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
rucaparib	●	●	●	●	● (III)
olaparib	●	●	●	○	● (II)
bevacizumab + olaparib	●	●	×	×	×
niraparib	●	●	×	×	● (II)
atezolizumab, chemotherapy, niraparib	×	×	×	×	● (III)
cediranib, olaparib	×	×	×	×	● (III)
atezolizumab	×	×	×	×	● (II)
berzosertib	×	×	×	×	● (II)
ceralasertib, olaparib	×	×	×	×	● (II)
IMP4297	×	×	×	×	● (II)
olaparib, chemotherapy	×	×	×	×	● (II)
olaparib, talazoparib	×	×	×	×	● (II)
talazoparib	×	×	×	×	● (II)
AMXI-5001	×	×	×	×	● (I/II)
AT-406, nivolumab	×	×	×	×	● (I/II)
BAY-1895344	×	×	×	×	● (I/II)
durvalumab + olaparib + tremelimumab	×	×	×	×	● (I/II)
enapotamab vedotin	×	×	×	×	● (I/II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



Relevant Therapy Summary (continued)

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ✕ No evidence

BRCA1 p.(Q1742*) c.5224C>T (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
RP-3500, talazoparib	✕	✕	✕	✕	● (I/II)
rucaparib, nivolumab, ipilimumab	✕	✕	✕	✕	● (I/II)
BAY-1895344, niraparib	✕	✕	✕	✕	● (I)
copanlisib, olaparib, durvalumab	✕	✕	✕	✕	● (I)
HWH-340	✕	✕	✕	✕	● (I)
mirvetuximab, rucaparib	✕	✕	✕	✕	● (I)
olaparib, adavosertib	✕	✕	✕	✕	● (I)

* 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 2020-10-14. For the most up-to-date information, search www.fda.gov.

BRCA1 p.(Q1742*) c.5224C>T

① olaparib, bevacizumab + olaparib

Cancer type: Ovarian Cancer, Prostate Cancer **Label as of:** 2020-05-19

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.
- 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/2020/208558s014lbl.pdf



BRCA1 p.(Q1742*) c.5224C>T (continued)

① rucaparib

Cancer type: Ovarian Cancer, Prostate Cancer **Label as of:** 2020-05-15

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.
- 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.

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/2020/209115s004lbl.pdf

● niraparib

Cancer type: Ovarian Cancer

Label as of: 2020-04-29

Variant class: BRCA1 mutation

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 three 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 six 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/2020/208447s015s017lbl.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 2020-10-01. 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.(Q1742*) c.5224C>T

● bevacizumab + olaparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer; Stage II, III, IV; Post-primary therapy, with bevacizumab used during primary therapy; Partial or complete remission (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2020]

● niraparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer; Stage II, III, IV; Post-primary therapy, with no bevacizumab during primary therapy; Partial or complete remission (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2020]

● olaparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer; Stage II, III, IV; Post-primary therapy, with no bevacizumab during primary therapy; Partial or complete remission (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2020]



BRCA1 p.(Q1742*) c.5224C>T (continued)

● niraparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer; Stage II, III, IV; Post-primary therapy, with bevacizumab used during primary therapy; Partial or complete remission (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2020]

● olaparib

Cancer type: Ovarian Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer; Stage II, III, IV; Post-primary therapy, with bevacizumab used during primary therapy; Partial or complete remission (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2020]

● rucaparib

Cancer type: Ovarian Cancer

Variant class: BRCA mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer; Platinum-Sensitive or Resistant (Recurrence therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2020]

○ olaparib

Cancer type: Prostate Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Castration Resistant Prostate Adenocarcinoma; M1; Prior therapy of abiraterone/enzalutamide (Second-line therapy) (Useful in certain circumstances)
- Castration Resistant Prostate Adenocarcinoma; M1 (Subsequent therapy) (Useful in certain circumstances)

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 2.2020]



BRCA1 p.(Q1742*) c.5224C>T (continued)

☐ rucaparib

Cancer type: Prostate Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Castration Resistant Prostate Adenocarcinoma; M1; Prior therapy of abiraterone, enzalutamide or docetaxel (Second-line therapy) (Useful in certain circumstances)
- Castration Resistant Prostate Adenocarcinoma; M1 (Subsequent therapy) (Useful in certain circumstances)

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 2.2020]

☐ olaparib

Cancer type: Prostate Cancer

Variant class: BRCA1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Castration Resistant Prostate Adenocarcinoma; M1; Prior therapy of docetaxel (Second-line therapy) (Useful in certain circumstances)

Reference: NCCN Guidelines® - NCCN-Prostate Cancer [Version 2.2020]



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 2020-10-14. For the most up-to-date information, search www.ema.europa.eu/ema.

BRCA1 p.(Q1742*) c.5224C>T

● olaparib

Cancer type: Ovarian Cancer

Label as of: 2020-10-06

Variant class: BRCA1 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: 2019-05-24

Variant class: BRCA1 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 2020-10-01. For the most up-to-date information, search www.esmo.org.

BRCA1 p.(Q1742*) c.5224C>T

☒ rucaparib

Cancer type: Ovarian Cancer

Variant class: BRCA mutation

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

Population segment (Line of therapy):

- Recurrent Platinum-Sensitive Ovarian Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

☐ olaparib

Cancer type: Prostate Cancer

Variant class: BRCA1 mutation

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

Population segment (Line of therapy):

- Metastatic Castration-Resistant Prostate Cancer; Progressed on prior new hormonal agent therapy (Not Specified)

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



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/2020/208558s014lbl.pdf
20. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/209115s004lbl.pdf
21. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/211651s005lbl.pdf
22. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208447s015s017bledt.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