

ACT Onco[®] + Report

PATIENT		
Identifier: 郭福屏		Patient ID: 22079523
Date of Birth: Jan 28, 1951		Gender: Male
Diagnosis: Metastatic adenocarcinoma		
ORDERING PHYSICIAN		
Name: 陳育民醫師		Tel: 886-228712121
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SPECIMEN		
Specimen ID: S11237011A	Collection site: Cerebrum	Type: FFPE tissue
Date received: Aug 11, 2023	Lab ID: AA-23-05282	D/ID: NA

ABOUT ACT Onco[®]+

The test is a next-generation sequencing (NGS)-based assay developed for efficient and comprehensive genomic profiling of cancers. This test interrogates coding regions of 440 genes associated with cancer treatment, prognosis and diagnosis. Genetic mutations detected by this test include small-scale mutations like single nucleotide variants (SNVs), small insertions and deletions (InDels) (≤ 15 nucleotides) and large-scale genomic alterations like copy number alterations (CNAs). The test also includes an RNA test, detecting fusion transcripts of 13 genes.

SUMMARY FOR ACTIONABLE VARIANTS

VARIANTS/BIOMARKERS WITH EVIDENCE OF CLINICAL SIGNIFICANCE

Genomic Alterations/Biomarkers	Probable Effects in Patient's Cancer Type		Probable Sensitive in Other Cancer Types
	Sensitive	Resistant	
EGFR L858R	-	-	Afatinib, Dacomitinib, Erlotinib, Gefitinib, Osimertinib

VARIANTS/BIOMARKERS WITH POTENTIAL CLINICAL SIGNIFICANCE

Genomic Alterations/Biomarkers	Possibly Sensitive	Possibly Resistant
CCND3 Amplification	Abemaciclib	-
VEGFA Amplification	Sorafenib	-

Note:

- The above summary tables present genomic variants and biomarkers based on the three-tiered approach proposed by US FDA for reporting tumor profiling NGS testing. "Variants/biomarkers with evidence of clinical significance" refers to mutations that are widely recognized as standard-of-care biomarkers (FDA level 2/AMP tier 1). "Variants/biomarkers with potential clinical significance" refers to mutations that are not included in the standard of care but are informational for clinicians, which are commonly biomarkers used as inclusion criteria for clinical trials (FDA level 3/AMP tier 2).
- The therapeutic agents and possible effects to a given drug are based on mapping the variants/biomarkers with ACT Genomics clinical knowledge database. The mapping results only provide information for reference, but not medical recommendation.
- Please refer to corresponding sections for more detailed information about genomic alteration and clinical relevance listed above.

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TESTING RESULTS

VARIANT(S) WITH CLINICAL RELEVANCE

- Single Nucleotide and Small InDel Variants

Gene	Amino Acid Change	Allele Frequency
CTNNB1	S37C	34.4%
CTNNB1	K335T	34.1%
EGFR	L858R	25.3%

- Copy Number Alterations

Chromosome	Gene	Variation	Copy Number
Chr13	BRCA2	Heterozygous deletion	1
Chr6	E2F3	Amplification	6
Chr6	CCND3, HSP90AB1, VEGFA	Amplification	7
Chr5	TERT	Amplification	10
Chr6	ROS1	Amplification	10

- Fusions

Fusion Gene & Exon	Transcript ID
No fusion gene detected in this sample	

- Immune Checkpoint Inhibitor (ICI) Related Biomarkers

Biomarker	Results
Tumor Mutational Burden (TMB)	1.3 muts/Mb
Microsatellite Instability (MSI)	Microsatellite stable (MSS)

Note:

- Variant(s) enlisted in the SNV table may currently exhibit no relevance to treatment response prediction. Please refer to INTERPRETATION for more biological information and/or potential clinical impacts of the variants.
- Loss of heterozygosity (LOH) information was used to infer tumor cellularity. Copy number alteration in the tumor was determined based on 50% tumor purity.
- For more therapeutic agents which are possibly respond to heterozygous deletion of genes listed above, please refer to APPENDIX for more information.
- TMB was calculated by using the sequenced regions of ACTOnco[®] to estimate the number of somatic nonsynonymous mutations per megabase of all protein-coding genes (whole exome). The threshold for high mutation load is set at ≥ 7.5 mutations per megabase. TMB, microsatellite status and gene copy number deletion cannot be determined if calculated tumor purity is $< 30\%$.

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THERAPEUTIC IMPLICATIONS TARGETED THERAPIES

Genomic Alterations	Therapies	Effect
Level 3A		
EGFR L858R	Afatinib, Dacomitinib, Erlotinib, Gefitinib, Osimertinib	sensitive
Level 3B		
CCND3 Amplification	Abemaciclib	sensitive
Level 4		
VEGFA Amplification	Sorafenib	sensitive

Therapies associated with benefit or lack of benefit are based on biomarkers detected in this tumor and published evidence in professional guidelines or peer-reviewed journals.

Level	Description
1	FDA-recognized biomarkers predictive of response or resistance to FDA approved drugs in this indication
2	Standard care biomarkers (recommended by the NCCN guideline) predictive of response or resistance to FDA approved drugs in this indication
3A	Biomarkers predictive of response or resistance to therapies approved by the FDA or NCCN guideline in a different cancer type
3B	Biomarkers that serve as inclusion criteria for clinical trials (minimal supportive data required)
4	Biomarkers that show plausible therapeutic significance based on small studies, few case reports, or preclinical studies

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IMMUNE CHECKPOINT INHIBITORS (ICIs)

No genomic alterations detected to confer sensitivity or lack of benefit to immune checkpoint therapies.

- Other Biomarkers with Potential Clinical Effects for ICIs

Genomic Alterations	Potential Clinical Effects
EGFR aberration	Likely associated with WORSE response to ICIs

Note: Tumor non-genomic factors, such as patient germline genetics, PDL1 expression, tumor microenvironment, epigenetic alterations or other factors not provided by this test may affect ICI response.

CHEMOTHERAPIES

No genomic alterations detected in this tumor predicted to confer sensitivity or lack of benefit to chemotherapies.

HORMONAL THERAPIES

No genomic alterations detected in this tumor predicted to confer sensitivity or lack of benefit to hormonal therapies.

OTHERS

No genomic alterations detected in this tumor predicted to confer sensitivity or lack of benefit to other therapies.

Note:

Therapeutic implications provided in the test are based solely on the panel of 440 genes sequenced. Therefore, alterations in genes not covered in this panel, epigenetic and post-transcriptional and post-translational factors may also determine a patient's response to therapies. In addition, several other patient-associated clinical factors, including but not limited to, prior lines of therapies received, dosage and combinations with other therapeutic agents, patient's cancer types, sub-types, and/or stages, may also determine the patient's clinical response to therapies.

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VARIANT INTERPRETATION

CTNNB1 K335T, S37C

Biological Impact

The CTNNB1 gene encodes for the β -catenin, a transcriptional activator involves in the canonical Wnt signaling pathway^{[1][2]}. β -catenin also regulates cyclin D1 and MYC expression, which play important roles in cancer development^{[3][4]}. Mutations of CTNNB1 are common in a wide range of solid tumors, including liver, endometrial, colorectal, and lung cancer^{[5][6][7][8][9][10]}. CTNNB1 mutations are more frequently found in hepatocellular carcinomas (HCCs) patients without hepatitis B virus (HBV) infection, which is mostly developed on the well-differentiated, noncirrhotic liver, and displayed cholestasis^{[11][12][13][14]}. Of note, the majority of CTNNB1 alterations identified in cancers are missense mutations and all of which localize in the hotspot exon 3 at S33, S37, S45, T41, D32, and G34^{[15][16]}.

CTNNB1 K335T lies within ARM repeat 5 of the β -catenin protein (UniProtKB). K335T confers a gain of function to the β -catenin protein as demonstrated by increased protein activity and loss of APC binding *in vitro*^[17].

CTNNB1 S37C lies within the ubiquitination recognition motif of the β -catenin protein. Mutation at the S37 residue abolish the phosphorylation of β -catenin by GSK3 β and may lead to deregulated accumulation of β -catenin^{[16][18]}. S37C and S37F mutations have been observed in ovarian cancer and were demonstrated as an oncogenic mutation with elevated nuclear accumulation of β -catenin protein^[19].

Therapeutic and prognostic relevance

In a retrospective study, patients with desmoid fibromatosis harboring CTNNB1 activating mutations such as S45F/N/P or T41A demonstrated a greater progression arrest rate (PAR) at 6 months compared to patients with wild-type CTNNB1 when treated with imatinib, a multi-target inhibitor of c-KIT, PDGFR, and BCR-ABL^[20].

Results from a Phase II study of temsirolimus-containing regimens in advanced endometrial cancer (EC) showed that CTNNB1 exon 3 mutations were associated with longer PFS on temsirolimus^[21]. Besides, three patients with recurrent endometrial carcinoma harboring CTNNB1 mutations on exon 3 (one is D32V, another is S37Y, and the other is both H36Y and S37C) also responded well to everolimus and letrozole, based on the results of a Phase II study^[22].

WNT-driven medulloblastomas, which harboring CTNNB1 activating mutations, are associated with favorable prognosis^{[23][24]}. Low expression of CTNNB1 has been reported to associate with longer overall survival in low-grade endometrioid endometrial carcinoma (EEC)^[25].

EGFR L858R

Biological Impact

The EGFR gene encodes for the Epidermal Growth Factor Receptor, a receptor tyrosine kinase which binds to its ligands, including Epidermal Growth Factor (EGF) and Transforming Growth Factor- α (TGF- α), activates downstream signaling pathways, including the canonical oncogenic MAPK and PI3K/AKT/mTOR signaling cascades^[26]. Increased EGFR activity by mutations and/or amplification of the EGFR gene has been described in a wide range of cancers, such as lung, brain, colorectal and head and neck cancer^[27]. Mutations in the kinase domain of EGFR are commonly observed in non-small cell lung cancer (NSCLC), resulting in a constitutively activated form of the receptor^[28]. On the other hand, in the brain and colorectal cancers, the most prevalent EGFR alteration is copy number amplification that results in receptor overexpression^[29].

EGFR L858R is a missense mutation at position 858, located in exon 21, which encodes part of the kinase domain, from a leucine to an arginine residue^[30]. The two most common EGFR alterations, L858R mutation and exon 19 deletions can result in constitutive activation of signal transduction pathways, leading to cell proliferation or anti-apoptosis without ligand binding^[31].

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Therapeutic and prognostic relevance

There is accumulated clinical evidence suggested that patients with MDM2/MDM4 amplification or EGFR aberrations exhibited poor clinical outcome and demonstrated a significantly increased rate of tumor growth (hyper-progression) after receiving immune checkpoint (PD-1/PD-L1) inhibitors therapies^[32](Annals of Oncology (2017) 28 (suppl_5): v403-v427. 10.1093/annonc/mdx376).

EGFR mutation has been determined as an inclusion criteria for the trials examining afatinib efficacy in malignant glioma and pediatric tumors (NCT02423525, NCT02372006). The first- and second-generation EGFR-TKIs, including dacomitinib, erlotinib, gefitinib, and afatinib, have been approved by the U.S. FDA as first-line treatments for non-small cell lung cancer patients with EGFR exon 19 deletion or L858R mutation. Osimertinib, a third-generation EGFR-TKI, has also been approved by the U.S. FDA. It is indicated for adjuvant treatment or first-line treatment of metastatic NSCLC patients with EGFR exon 19 deletion or L858R mutation.

A phase III trial (NCT01774721) show that dacomitinib significantly improved PFS over gefitinib in first-line treatment of patients with EGFR-mutation-positive NSCLC^[33]. Another phase III trial (NCT00949650) demonstrated that median PFS among lung cancer patients with exon 19 deletion or L858R EGFR mutation (n=308) was 13.6 months for afatinib and 6.9 months for chemotherapy^[34]. Results from a double-blind, phase 3 trial further showed that osimertinib significantly demonstrated longer PFS than standard EGFR-TKIs (18.9 months vs. 10.2 months) in previously untreated EGFR mutation-positive (exon 19 deletion or L858R) advanced NSCLC^[35].

BRCA2 Heterozygous deletion

Biological Impact

The BRCA2 gene encodes a tumor suppressor involved in the homologous recombination pathway for double-strand DNA repair^[36]. BRCA2 has been implicated as a haploinsufficient gene with one copy loss may lead to weak protein expression and is insufficient to execute its original physiological functions^[37]. BRCA2 germline mutations confer an increased lifetime risk of developing breast, ovarian, prostate and pancreatic cancer, limited reports of related gastric cancer, and Fanconi anemia subtype D1-associated risk of brain cancer, medulloblastoma, pharyngeal cancer, chronic lymphocytic leukemia and acute myeloid leukemia^[38]. Somatic mutations in BRCA2 are highest in colorectal, non-small cell lung cancer (NSCLC), and ovarian cancers^[39].

Therapeutic and prognostic relevance

Multiple PARP inhibitors, including olaparib, rucaparib, niraparib, and talazoparib, have been approved by the U.S. FDA for the treatment of cancer. Olaparib is approved for multiple settings in advanced ovarian cancer, metastatic breast cancer with BRCA mutations, metastatic pancreatic cancer, and mCRPC with BRCA mutations or HRR gene mutations, including BRCA mutations. Rucaparib is approved for maintenance treatment of recurrent ovarian cancer with BRCA mutations and mCRPC with BRCA mutations. Niraparib is approved for maintenance treatment of advanced ovarian cancer and recurrent ovarian cancer with BRCA mutations, and mCRPC with BRCA mutations in combination with abiraterone acetate. Talazoparib is approved for locally advanced or metastatic breast cancer with BRCA mutations and mCRPC with HRR gene mutations, including BRCA2.

According to the NCCN guidelines, rucaparib is recommended as recurrence therapy for patients with BRCA-mutated ovarian cancer who have been treated with multiple lines of chemotherapy. It is also recommended as maintenance therapy for patients with metastatic pancreatic cancer who have undergone prior platinum-based therapy and harbor germline or somatic BRCA mutations. Additionally, niraparib is recommended as maintenance therapy for ovarian cancer patients with BRCA mutations.

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CCND3 Amplification

Biological Impact

The cyclin D3 (CCND3) is one of the D-type cyclins, which expresses in the G1 phase of the cell cycle and promote the progression from G1 to S phase by binding to and activating the cyclin-dependent kinases CDK4 and CDK6^[40]. Amplification or increased expression of CCND3 has been demonstrated to cause loss of cell cycle control in human malignant gliomas^[41]. CCND3 upregulation is associated with liver metastasis in colorectal cancer^[42].

Therapeutic and prognostic relevance

In a retrospective study (n=50), an elevated on-treatment expression of CCND3 was found to be associated with neoadjuvant palbociclib resistance in estrogen receptor positive (ER+) breast cancer patients^[43]. However, another study showed that tumor cells harboring CCND2 and CCND3 gene amplification were sensitive to abemaciclib treatment and showed evidence of tumor regression in vivo (Cancer Res 2015;75(15 Suppl):Abstract nr 3104). CCND3 overexpression was significantly associated with poor overall survival and relapse-free survival in indolent lymphoma^[44]. CCND3 gene amplification is a marker of aggressiveness in bladder urothelial carcinoma to predict tumor progression^[45]. CCND3 amplification has been selected as an inclusion criteria for the trial examining CDK4/6 inhibitors abemaciclib, palbociclib, and ribociclib in different type of malignant solid tumor (NCT02187783, NCT04116541, NCT03310879, NCT04040205, NCT03526250, and NCT02154490).

E2F3 Amplification

Biological Impact

The E2F3 gene encodes a transcription factor that interacts directly with the retinoblastoma protein (pRB) to regulate the expression of genes involved in the cell cycle and DNA replication^{[46][47][48]}.

Amplification or overexpression of E2F3 has been reported in various types of cancers, including bladder cancer, hepatocellular carcinoma, retinoblastomas, and melanoma^{[49][50][51][52][53]}.

Therapeutic and prognostic relevance

A tissue microarray analysis indicated that amplification of the E2F3 gene is associated with increased E2F3 protein overexpression, accelerated cell proliferation, and poor prognosis in bladder cancer^[50]. Besides, elevated E2F genes and E2F transcriptional targets in tumors have been linked with poor prognosis in the liver and pancreatic cancers^[48].

HSP90AB1 Amplification

Biological Impact

HSP90AB1 (heat shock protein 90 kDa alpha, class B, member 1), also known as Hsp90beta, belonged to the heat shock protein family which function as molecular chaperones^[54]. Heat shock protein 90 (Hsp90) is a molecular chaperone that is induced in response to cellular stress. Hsp90 stabilizes client proteins involved in the cell cycle, proliferation, migration, and apoptosis^[55]. Hsp90 family has four major members including Hsp90alpha, Hsp90beta, GRP94, and Hsp75^[56].

Therapeutic and prognostic relevance

Results of human hepatocellular carcinoma tumor xenografts study showed that Hsp90beta promoted endothelial cell-dependent tumor angiogenesis in hepatocellular carcinoma^[56]. Amplification and high-level expression of HSP90AB1 were associated with poor prognosis in HER2 negative breast cancer patients^[57].

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ROS1 Amplification

Biological Impact

The ROS1 gene encodes a receptor tyrosine kinase^[58]. ROS1 gene rearrangements, which the kinase domain is retained^[59], are implicated in a range of human epithelial cancers including cholangiocarcinoma^[60], ovarian carcinoma^[61], gastric carcinoma^[62], angiosarcoma^[63], and most commonly non-small cell lung cancer^[64].

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Therapeutic and prognostic relevance

Crizotinib and entrectinib are FDA-approved for ROS1-positive metastatic NSCLC. The NCCN guidelines recommend ceritinib, crizotinib, and entrectinib in the first-line setting for patients with advanced ROS1-rearranged NSCLC, and lorlatinib and entrectinib for subsequent therapy.

Lorlatinib, ceritinib, cabozantinib, brigatinib, and DS-6051b have shown clinical activity and efficacy in patients with ROS1-rearranged lung cancer^{[65][66][67][68]}.

In a clinical study of pemetrexed-based chemotherapy efficacy, patients with ROS1-rearranged lung cancer had a better overall response rate compared with patients who carry other driver mutations, including EGFR mutations, KRAS mutations, and EML4-ALK fusion^[69].

The gain of ROS1 gene was suggested as an independent poor prognostic factor for DFS (HR=2.16) and OS (HR=2.53) in NSCLC patients^[70].

TERT Amplification

Biological Impact

The TERT gene encodes the catalytic subunit of telomerase, an enzyme that maintains telomere length and genomic integrity^[71]. Upregulation of TERT promotes cancer development and progression via modulation of Wnt-catenin and nuclear factor kappa B signaling^{[72][73]}, and mitochondrial RNA processing^[74]. Activating mutations in the TERT promoter have been identified in a number of cancer types including melanoma, hepatocellular carcinoma, urothelial carcinoma, medulloblastoma, and glioma whereas TERT gene amplification is implicated in lung cancer, cervical cancer, breast cancer, Merkel cell carcinoma, neuroblastoma and adrenocortical carcinoma^{[75][76][77][78][79]}.

Therapeutic and prognostic relevance

Imetelstat (GRN163L), a telomere inhibitor which has been shown to inhibit cell proliferation in various cancer cell lines and tumor xenografts is currently in clinical trials^[71].

TERT gene amplification is an independent poor prognostic marker for disease-free survival in non-small cell lung cancer (NSCLC) and breast cancer^{[80][81][82]}.

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VEGFA Amplification

Biological Impact

VEGFA encodes the vascular endothelial growth factor A (often referred to as VEGF) that belongs to a family of vascular endothelial growth factors (VEGFs) and platelet-derived growth factors (PDGFs). In tumor cells, VEGFA signaling is mediated by the receptor tyrosine kinases VEGFR-1 and VEGFR-2^[83]. Other types of receptors such as platelet-derived growth factor receptors (PDGFR) and neuropilins also contribute to VEGFA signaling^{[84][85][86]}. VEGFA acts as an oncogene to regulate survival tumor cells and also affects the function of nearby immune cells^[87] and fibroblasts^{[88][89]}. VEGFA amplification has been observed across several tumor types, including hepatocellular carcinoma, adenocarcinoma of the pancreas and intestine, large cell carcinoma of the lung, and in endometrium serous carcinoma^[90].

Therapeutic and prognostic relevance

In vivo data and retrospective analysis showed that hepatocellular carcinoma (HCC) bearing VEGFA genomic amplification is sensitive to sorafenib treatment^[91]. VEGFA amplification has been used as an inclusion criteria for a trial evaluating bevacizumab efficacy in TNBC (NCT02101385), however, HER2+ or triple-negative breast cancer (TNBC) patients with a VEGFA-amplified tumor who received paclitaxel plus bevacizumab demonstrated poor outcomes, based on data from a retrospective study^[92]. Also, clinical studies suggested that overexpression of VEGFA was correlated with poor survival during bevacizumab therapy in NSCLC and glioblastoma^{[93][94][95][95]}.

Bevacizumab and aflibercept are FDA-approved anti-VEGF drugs for metastatic colorectal cancer^{[96][97]}. A clinical study showed that low post-therapeutic VEGF expression and decreased peri-therapeutic VEGF expression could be a predictor of responsiveness to first-line FOLFIRI plus bevacizumab treatment in metastatic colorectal cancer (mCRC) patients^[98].

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US FDA-APPROVED DRUG(S)

Abemaciclib (VERZENIO)

Abemaciclib is a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor. Abemaciclib is developed and marketed by Eli Lilly under the trade name VERZENIO.

- FDA Approval Summary of Abemaciclib (VERZENIO)

MONARCH E NCT03155997	Breast cancer (Approved on 2021/10/12)
	HR+/HER2- Abemaciclib + tamoxifen/aromatase inhibitor vs. Tamoxifen/aromatase inhibitor [IDFS at 36 months(%): 86.1 vs. 79.0]
MONARCH 3^[99] NCT02246621	Breast cancer (Approved on 2018/02/26)
	HR+/HER2- Abemaciclib + anastrozole/letrozole vs. Placebo + anastrozole/letrozole [PFS(M): 28.2 vs. 14.8]
MONARCH 2^[100] NCT02107703	Breast cancer (Approved on 2017/09/28)
	HR+/HER2- Abemaciclib + fulvestrant vs. Placebo + fulvestrant [PFS(M): 16.4 vs. 9.3]
MONARCH 1^[101] NCT02102490	Breast cancer (Approved on 2017/09/28)
	HR+/HER2- Abemaciclib [ORR(%): 19.7 vs. 17.4]

Afatinib (GILOTRIF)

Afatinib acts as an irreversible covalent inhibitor of the ErbB family of receptor tyrosine kinases, including epidermal growth factor receptor (EGFR) and erbB-2 (HER2). Afatinib is developed and marketed by Boehringer Ingelheim under the trade name GILOTRIF (United States) and GIOTRIF (Europe).

- FDA Approval Summary of Afatinib (GILOTRIF)

LUX-Lung 8^[102] NCT01523587	Non-small cell lung carcinoma (Approved on 2016/04/15)
	EGFR ex19del or L858R Afatinib vs. Erlotinib [PFS(M): 2.4 vs. 1.9]
LUX-Lung 3^[103] NCT00949650	Non-small cell lung carcinoma (Approved on 2013/07/13)
	EGFR ex19del or L858R Afatinib vs. Pemetrexed + cisplatin [PFS(M): 11.1 vs. 6.9]

Dacomitinib (VIZIMPRO)

Dacomitinib is an oral kinase inhibitor that targets EGFR. Dacomitinib is developed and marketed by Pfizer under the trade name VIZIMPRO.

- FDA Approval Summary of Dacomitinib (VIZIMPRO)

ARCHER 1050^[33] NCT01774721	Non-small cell lung carcinoma (Approved on 2018/09/27)
	EGFR ex19del or L858R Dacomitinib vs. Gefitinib [PFS(M): 14.7 vs. 9.2]

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Erlotinib (TARCEVA)

Erlotinib is a small molecule, reversible inhibitor of epidermal growth factor receptor (EGFR), a receptor tyrosine kinase. Erlotinib is developed by OSI Pharmaceuticals, Genentech and Roche, and marketed by Astellas Pharm Global Development under the trade name TARCEVA.

- FDA Approval Summary of Erlotinib (TARCEVA)

RELAY NCT02411448	Non-small cell lung carcinoma (Approved on 2020/05/29)
	EGFR ex19del or L858R Erlotinib + ramucirumab vs. Erlotinib + placebo [PFS(M): 19.4 vs. 12.4]
EURTAC^[104] NCT00446225	Non-small cell lung carcinoma (Approved on 2013/05/14)
	EGFR ex19del or L858R Erlotinib vs. Cisplatin + gemcitabine or cisplatin + docetaxel or carboplatin + gemcitabine or carboplatin + docetaxel [PFS(M): 10.4 vs. 5.2]
PA.3^[105] NCT00026338	Pancreatic cancer (Approved on 2005/11/02)
	- Gemcitabine vs. Placebo [OS(M): 6.4 vs. 6]

Gefitinib (IRESSA)

Gefitinib is a small molecule inhibitor of epidermal growth factor receptor (EGFR), a receptor tyrosine kinase. Gefitinib is developed and marketed by AstraZeneca under the trade name IRESSA.

- FDA Approval Summary of Gefitinib (IRESSA)

IFUM^[106] NCT01203917	Non-small cell lung carcinoma (Approved on 2015/07/13)
	EGFR ex19del or L858R Gefitinib [ORR(%): 50.0]

Niraparib (ZEJULA)

Niraparib is an oral, small molecule inhibitor of the DNA repair enzyme poly (ADP-ribose) polymerase-1 and -2 (PARP-1, -2). Niraparib is developed and marketed by Tesaro under the trade name ZEJULA.

- FDA Approval Summary of Niraparib (ZEJULA)

MAGNITUDE NCT03748641	Prostate cancer (Approved on 2023/08/11)
	BRCA mutation Niraparib and abiraterone acetate plus prednisone vs. placebo and abiraterone acetate plus prednisone [rPFS(M): 16.6 vs. 10.9]
PRIMA NCT02655016	Ovarian cancer, Fallopian tube cancer, Peritoneal carcinoma (Approved on 2020/04/29)
	- Niraparib vs. Placebo [PFS (overall population)(M): 13.8 vs. 8.2]
NOVA^[107] NCT01847274	Ovarian cancer, Fallopian tube cancer, Peritoneal carcinoma (Approved on 2017/03/27)
	- Niraparib vs. Placebo [PFS (overall population)(M): 11.3 vs. 4.7]

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Olaparib (LYNPARZA)

Olaparib is an oral, small molecule inhibitor of poly (ADP-ribose) polymerase-1, -2, and -3 (PARP-1, -2, -3). Olaparib is developed by KuDOS Pharmaceuticals and marketed by AstraZeneca under the trade name LYNPARZA.

- FDA Approval Summary of Olaparib (LYNPARZA)

PROpel NCT03732820	Prostate cancer (Approved on 2023/05/31)
	BRCA mutation Olaparib + abiraterone + prednisone vs. Placebo + abiraterone + prednisone [rPFS(M): not reached vs. 8]
OlympiA NCT02032823	Her2-negative high-risk early breast cancer (Approved on 2022/03/11)
	HER2-/gBRCA mutation Olaparib vs. Placebo [invasive disease-free survival (IDFS)(M):]
PROfound ^[108] NCT02987543	Prostate cancer (Approved on 2020/05/19)
	HRR genes mutation Olaparib vs. Enzalutamide or abiraterone acetate [PFS(M): 5.8 vs. 3.5]
PAOLA-1 ^[109] NCT02477644	Ovarian cancer (Approved on 2020/05/08)
	HRD+ Olaparib + bevacizumab vs. Placebo + bevacizumab [PFS(M): 37.2 vs. 17.7]
POLO ^[110] NCT02184195	Pancreatic adenocarcinoma (Approved on 2019/12/27)
	gBRCA mutation Olaparib vs. Placebo [ORR(%): 23.0 vs. 12.0, PFS(M): 7.4 vs. 3.8]
SOLO-1 ^[111] NCT01844986	Ovarian cancer, Fallopian tube cancer, Peritoneal carcinoma (Approved on 2018/12/19)
	gBRCA mutation or sBRCA mutation Olaparib vs. Placebo [PFS(M): NR vs. 13.8]
OlympiAD ^[112] NCT02000622	Breast cancer (Approved on 2018/02/06)
	HER2-/gBRCA mutation Olaparib vs. Chemotherapy [PFS(M): 7 vs. 4.2]
SOLO-2/ENGOT-Ov21 ^[113] NCT01874353	Ovarian cancer, Fallopian tube cancer, Peritoneal carcinoma (Approved on 2017/08/17)
	gBRCA mutation Olaparib vs. Placebo [PFS(M): 19.1 vs. 5.5]
Study19 ^[114] NCT00753545	Ovarian cancer, Fallopian tube cancer, Peritoneal carcinoma (Approved on 2017/08/17)
	- Olaparib vs. Placebo [PFS(M): 8.4 vs. 4.8]

Osimertinib (TAGRISSO)

Osimertinib is a third-generation tyrosine kinase inhibitor (TKI) for patients with tumors harboring EGFR T790M mutation. Osimertinib is developed and marketed by AstraZeneca under the trade name TAGRISSO.

- FDA Approval Summary of Osimertinib (TAGRISSO)

ADAURA NCT02511106	Non-small cell lung carcinoma (Approved on 2020/12/18)
	EGFR ex19del or L858R Osimertinib vs. Placebo + adjuvant chemotherapy [DFS(M): NR vs. 19.6]
FLAURA ^[35] NCT02296125	Non-small cell lung carcinoma (Approved on 2018/04/18)
	EGFR ex19del or L858R Osimertinib vs. Gefitinib or erlotinib [PFS(M): 18.9 vs. 10.2]

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AURA3 ^[115] NCT02151981	Non-small cell lung carcinoma (Approved on 2017/03/30)
	EGFR T790M
	Osimertinib vs. Chemotherapy [PFS(M): 10.1 vs. 4.4]
AURA ^[116] NCT01802632	Non-small cell lung carcinoma (Approved on 2015/11/13)
	EGFR T790M
	Osimertinib [ORR(%): 59.0]

Rucaparib (RUBRACA)

Rucaparib is an inhibitor of the DNA repair enzyme poly (ADP-ribose) polymerase-1, -2 and -3 (PARP-1, -2, -3). Rucaparib is developed and marketed by Clovis Oncology under the trade name RUBRACA.

- FDA Approval Summary of Rucaparib (RUBRACA)

TRITON2 NCT02952534	Prostate cancer (Approved on 2020/05/15)
	gBRCA mutation or sBRCA mutation
	Rucaparib [ORR(%): 44.0, DOR(M): NE]
ARIEL3 ^[117] NCT01968213	Ovarian cancer, Fallopian tube cancer, Peritoneal carcinoma (Approved on 2018/04/06)
	-
	Rucaparib vs. Placebo [PFS (All)(M): 10.8 vs. 5.4, PFS (HRD)(M): 13.6 vs. 5.4, PFS (tBRCA)(M): 16.6 vs. 5.4]

Sorafenib (NEXAVAR)

Sorafenib is a small molecule multi-kinase inhibitor that targets multiple kinase families including VEGFR, PDGFRB, and the RAF family kinases. Sorafenib is co-developed and co-marketed by Bayer HealthCare Pharmaceuticals and Onyx Pharmaceuticals under the trade name NEXAVAR.

- FDA Approval Summary of Sorafenib (NEXAVAR)

DECISION ^[118] NCT00984282	Differentiated thyroid carcinoma (Approved on 2013/11/22)
	-
	Sorafenib vs. Placebo [PFS(M): 10.8 vs. 5.8]
SHARP ^[119] NCT00105443	Hepatocellular carcinoma (Approved on 2007/11/16)
	-
	Sorafenib vs. Placebo [OS(M): 10.7 vs. 7.9]
TARGET ^[120] NCT00073307	Renal cell carcinoma (Approved on 2005/12/20)
	-
	Sorafenib vs. Placebo [PFS(D): 167 vs. 84]

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Talazoparib (TALZENNA)

Talazoparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1 and PARP2. Talazoparib is developed and marketed by Pfizer under the trade name TALZENNA.

- FDA Approval Summary of Talazoparib (TALZENNA)

TALAPRO-2 NCT03395197	Prostate cancer (Approved on 2023/06/20)
	HRR genes mutation
	Talazoparib + enzalutamide vs. Placebo + enzalutamide [rPFS(M): Not reached vs. 13.8]
EMBRACA ^[121] NCT01945775	Breast cancer (Approved on 2018/10/16)
	HER2-/gBRCA mutation
	Talazoparib vs. Chemotherapy [PFS(M): 8.6 vs. 5.6]

D=day; W=week; M=month

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ONGOING CLINICAL TRIALS

Trials were searched by applying filters: study status, patient's diagnosis, intervention, location and/or biomarker(s). Please visit <https://clinicaltrials.gov> to search and view for a complete list of open available and updated matched trials.

No trial has been found.

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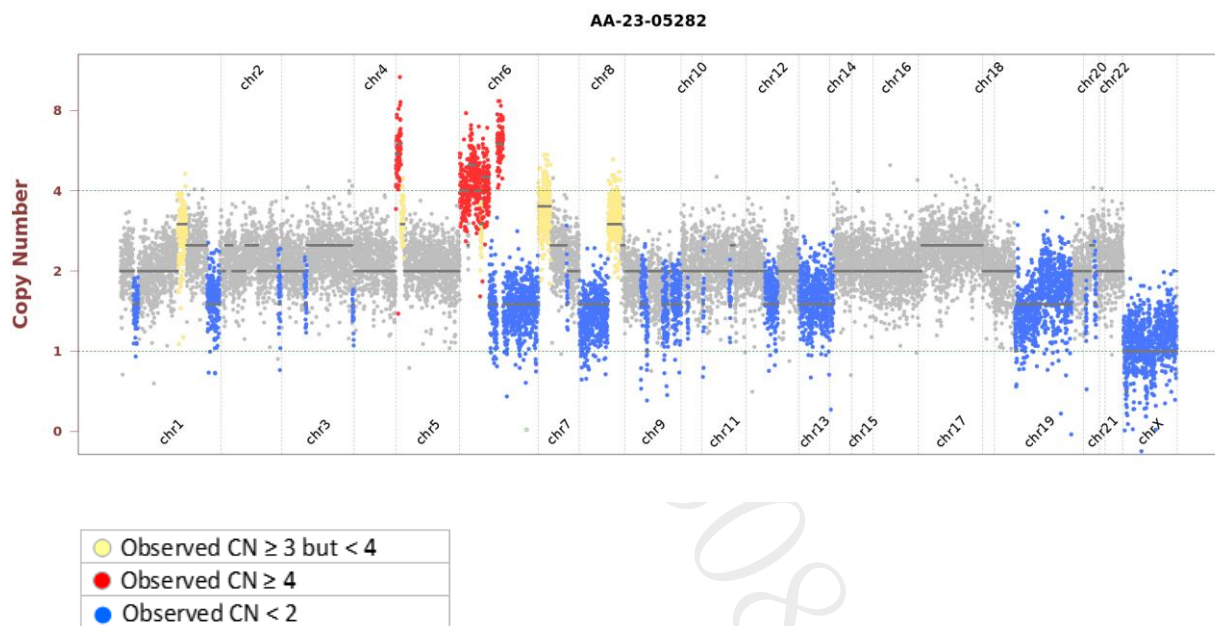
SUPPLEMENTARY INFORMATION OF TESTING RESULTS DETAILED INFORMATION OF VARIANTS WITH CLINICAL RELEVANCE

- Single Nucleotide and Small InDel Variants

Gene	Amino Acid Change	Exon	cDNA Change	Accession Number	COSMIC ID	Allele Frequency	Coverage
CTNNB1	K335T	7	c.1004A>C	NM_001904	COSM1725761	34.1%	604
CTNNB1	S37C	3	c.110C>G	NM_001904	COSM5679	34.4%	1494
EGFR	L858R	21	c.2573T>G	NM_005228	COSM6224	25.3%	3382

- Copy Number Alterations

Observed copy number (CN) for each evaluated position is shown on the y-axis. Regions referred to as amplification or deletion are shown in color. Regions without significant changes are represented in gray.



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OTHER DETECTED VARIANTS

Gene	Amino Acid Change	Exon	cDNA Change	Accession Number	COSMIC ID	Allele Frequency	Coverage
ABL2	F1134C	12	c.3401T>G	NM_007314	-	31.6%	1744
ADAMTS13	S1314L	28	c.3941C>T	NM_139025	-	19.5%	745
APC	S2296N	16	c.6887G>A	NM_000038	COSM1580517	13.8%	1086
ATR	Splice region	-	c.1885+7G>A	NM_001184	-	49.9%	401
CDK12	P650L	3	c.1949C>T	NM_016507	-	42.8%	348
CHEK2	R180C	4	c.538C>T	NM_007194	-	48.0%	1165
EP300	P1875S	31	c.5623C>T	NM_001429	-	47.2%	527
GRIN2A	L963F	14	c.2887C>T	NM_000833	COSM9359837	48.3%	1167
HSPA4	Splice region	-	c.307-3C>T	NM_002154	-	35.5%	1114
IDH2	Splice acceptor	-	c.535-2A>G	NM_002168	-	51.8%	884
MUC16	T11576M	5	c.34727C>T	NM_024690	-	43.5%	531
MUC16	T8900S	3	c.26698A>T	NM_024690	-	45.3%	685
PRKDC	Splice region	27	c.3045T>C	NM_006904	-	73.5%	663
RBM10	N306I	10	c.917A>T	NM_005676	-	67.3%	551

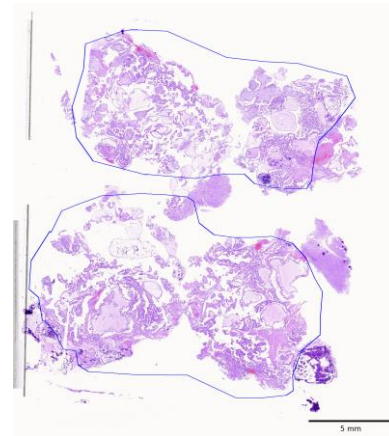
Note:

- This table enlists variants detected by the panel other than those with clinical relevance (reported in Testing Result section). The clinical impact of a genetic variant is determined according to ACT Genomics in-house clinical knowledge database. A negative result does not necessarily indicate absence of biological effect on the tumor. Some variants listed here may possibly have preclinical data or may show potential clinical relevance in the future.

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TEST DETAILS

SPECIMEN RECEIVED AND PATHOLOGY REVIEW



- Collection date: Jul 28, 2023
- Facility retrieved: 臺北榮總
- H&E-stained section No.: S11237011A
- Collection site: Cerebrum
- Examined by: Dr. Chien-Ta Chiang
 1. The percentage of viable tumor cells in total cells in the whole slide (%): 20%
 2. The percentage of viable tumor cells in total cells in the encircled areas in the whole slide (%): 40%
 3. The percentage of necrotic cells (including necrotic tumor cells) in total cells in the whole slide (%): 0%
 4. The percentage of necrotic cells (including necrotic tumor cells) in total cells in the encircled areas in the whole slide (%): 0%
 5. Additional comment: NA
- Manual macrodissection: Performed on the highlighted region
- The outline highlights the area of malignant neoplasm annotated by a pathologist.

RUN QC

- Panel: ACTOnco®+

DNA test

- Mean Depth: 982x
- Target Base Coverage at 100x: 95%

RNA test

- Average unique RNA Start Sites per control GSP2: 137

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LIMITATIONS

1. This test does not provide information of variant causality and does not detect variants in non-coding regions that could affect gene expression. This report does not report polymorphisms and we do not classify whether a mutation is germline or somatic. Variants identified by this assay were not subject to validation by Sanger or other technologies.
2. The possibility cannot be excluded that certain pathogenic variants detected by other sequencing tools may not be reported in the test because of technical limitation of bioinformatics algorithm or the NGS sequencing platform, e.g. low coverage.
3. This test has been designed to detect fusions in 13 genes sequenced. Therefore, fusion in genes not covered by this test would not be reported. For novel fusions detected in this test, Sanger sequencing confirmation is recommended if residue specimen is available.

NEXT-GENERATION SEQUENCING (NGS) METHODS

DNA test

Extracted genomic DNA was amplified using primers targeting coding exons of analyzed genes and subjected to library construction. Barcoded libraries were subsequently conjugated with sequencing beads by emulsion PCR and enriched using Ion Chef system. Sequencing was performed according to Ion Proton or Ion S5 sequencer protocol (Thermo Fisher Scientific).

Raw reads generated by the sequencer were mapped to the hg19 reference genome using the Ion Torrent Suite. Coverage depth was calculated using Torrent Coverage Analysis plug-in. Single nucleotide variants (SNVs) and short insertions/deletions (InDels) were identified using the Torrent Variant Caller plug-in. VEP (Variant Effect Predictor) was used to annotate every variant using databases from Clinvar, COSMIC and Genome Aggregation database. Variants with coverage ≥ 20 , allele frequency $\geq 5\%$ and actionable variants with allele frequency $\geq 2\%$ were retained. This test provides uniform coverage of the targeted regions, enabling target base coverage at $100\times \geq 85\%$ with a mean coverage $\geq 500\times$.

Variants reported in Genome Aggregation database with $> 1\%$ minor allele frequency (MAF) were considered as polymorphisms. ACT Genomics in-house database was used to determine technical errors. Clinically actionable and biologically significant variants were determined based on the published medical literature.

The copy number alterations (CNAs) were predicted as described below:

Amplicons with read counts in the lowest 5th percentile of all detectable amplicons and amplicons with a coefficient of variation ≥ 0.3 were removed. The remaining amplicons were normalized to correct the pool design bias. ONCOCNV (an established method for calculating copy number aberrations in amplicon sequencing data by Boeva et al., 2014) was applied for the normalization of total amplicon number, amplicon GC content, amplicon length, and technology-related biases, followed by segmenting the sample with a gene-aware model. The method was used as well for establishing the baseline of copy number variations.

Tumor mutational burden (TMB) was calculated by using the sequenced regions of ACTOnco[®] to estimate the number of somatic nonsynonymous mutations per megabase of all protein-coding genes (whole exome). The TMB calculation predicted somatic variants and applied a machine learning model with a cancer hotspot correction. TMB may be reported as "TMB-High", "TMB-Low" or "Cannot Be Determined". TMB-High corresponds to ≥ 7.5 mutations per megabase (Muts/Mb); TMB-Low corresponds to < 7.5 Muts/Mb. TMB is reported as "Cannot Be Determined" if the tumor purity of the sample is $< 30\%$.

Classification of microsatellite instability (MSI) status is determined by a machine learning prediction algorithm. The change of a number of repeats of different lengths from a pooled microsatellite stable (MSS) baseline in > 400 genomic loci are used as the features for the algorithm. The final output of the results is either microsatellite Stable (MSS) or microsatellite instability high (MSI-H).

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RNA test

Extracted RNA was reverse-transcribed and subjected to library construction. Sequencing was performed according to Ion Proton or Ion S5 sequencer protocol (Thermo Fisher Scientific). To ensure sequencing quality for fusion variant analysis, the average unique RNA Start Sites (SS) per control Gene Specific Primer 2 (GSP 2) should be ≥ 10 .

The fusion analysis pipeline aligned sequenced reads to the human reference genome, identified regions that map to noncontiguous regions of the genome, applied filters to exclude probable false-positive events and, annotated previously characterized fusion events according to Quiver Gene Fusion Database, a curated database owned and maintained by ArcherDX. In general, samples with detectable fusions need to meet the following criteria: (1) Number of unique start sites (SS) for the GSP2 ≥ 3 ; (2) Number of supporting reads spanning the fusion junction ≥ 5 ; (3) Percentage of supporting reads spanning the fusion junction $\geq 10\%$; (4) Fusions annotated in Quiver Gene Fusion Database.

DATABASE USED

- Reference genome: Human genome sequence hg19
- COSMIC v.92
- Genome Aggregation database r2.1.1
- ClinVar (version 20210404)
- ACT Genomics in-house database
- Quiver Gene Fusion Database version 5.1.18

Variant Analysis:

醫檢師張筑芃 博士
Chu-Yuan Chang Ph.D.
檢字第 020115 號



Sign Off

解剖病理專科醫師王業翰
Yeh-Han Wang M.D.
病解字第 000545 號



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GENE LIST SNV & CNV

ABCB1*	ABCC2*	ABCG2*	ABL1	ABL2	ADAMTS1	ADAMTS13	ADAMTS15	ADAMTS16	ADAMTS18	ADAMTS6	ADAMTS9
ADAMTSL1	ADGRA2	ADH1C*	AKT1	AKT2	AKT3	ALDH1A1*	ALK	AMER1	APC	AR	ARAF
ARID1A	ARID1B	ARID2	ASXL1	ATM	ATR	ATRX	AURKA	AURKB	AXIN1	AXIN2	AXL
B2M	BAP1	BARD1	BCL10	BCL2*	BCL2L1	BCL2L2*	BCL6	BCL9	BCOR	BIRC2	BIRC3
BLM	BMPR1A	BRAF	BRCA1	BRCA2	BRD4	BRIP1	BTG1	BTG2*	BTB	BUB1B	CALR
CANX	CARD11	CASP8	CBFB	CBL	CCNA1	CCNA	CCNB1	CCNB2	CCNB3	CCND1	CCND2
CCND3	CCNE1	CCNE2	CCNH	CD19	CD274	CD58	CD70*	CD79A	CD79B	CDC73	CDH1
CDK1	CDK12	CDK2	CDK4	CDK5	CDK6	CDK7	CDK8	CDK9	CDKN1A	CDKN1B	CDKN2A
CDKN2B	CDKN2C	CEBPA*	CHEK1	CHEK2	CIC	CREBBP	CRKL	CRLF2	CSF1R	CTCF	CTLA4
CTNNA1	CTNNB1	CUL3	CYLD	CYP1A1*	CYP2B6*	CYP2C19*	CYP2C8*	CYP2D6	CYP2E1*	CYP3A4*	CYP3A5*
DAXX	DCUN1D1	DDR2	DICER1	DNMT3A	DOT1L	DPYD	DTX1	E2F3	EGFR	EP300	EPCAM
EPHA2	EPHA3	EPHA5	EPHA7	EPHB1	ERBB2	ERBB3	ERBB4	ERCC1	ERCC2	ERCC3	ERCC4
ERCC5	ERG	ESR1	ESR2	ETV1	ETV4	EZH2	FAM46C	FANCA	FANCC	FANCD2	FANCE
FANCF	FANCG	FANCL	FAS	FAT1	FBXW7	FCGR2B	FGF1*	FGF10	FGF14	FGF19*	FGF23
FGF3	FGF4*	FGF6	FGFR1	FGFR2	FGFR3	FGFR4	FH	FLCN	FLT1	FLT3	FLT4
FOXL2*	FOXP1	FRG1	FUBP1	GATA1	GATA2	GATA3	GNA11	GNA13	GNAQ	GNAS	GREM1
GRIN2A	GSK3B	GSTP1*	GSTT1*	HGF	HIF1A	HIST1H1C*	HIST1H1E*	HNF1A	HR	HRAS*	HSP90AA1
HSP90AB1	HSPA4	HSPA5	IDH1	IDH2	IFNL3*	IGF1	IGF1R	IGF2	IKBKB	IKBKE	IKZF1
IL6	IL7R	INPP4B	INSR	IRF4	IRS1	IRS2*	JAK1	JAK2	JAK3	JUN*	KAT6A
KDM5A	KDM5C	KDM6A	KDR	KEAP1	KIT	KMT2A	KMT2C	KMT2D	KRAS	LCK	LIG1
LIG3	LMO1	LRP1B	LYN	MALT1	MAP2K1	MAP2K2	MAP2K4	MAP3K1	MAP3K7	MAPK1	MAPK3
MAX	MCL1	MDM2	MDM4	MED12	MEF2B	MEN1	MET	MITF	MLH1	MPL	MRE11
MSH2	MSH6	MTHFR*	MTOR	MUC16	MUC4	MUC6	MUTYH	MYC	MYCL	MYCN	MYD88
NAT2*	NBN	NEFH	NF1	NF2	NFE2L2	NFKB1	NFKBIA	NKX2-1*	NOTCH1	NOTCH2	NOTCH3
NOTCH4	NPM1	NQO1*	NRAS	NSD1	NTRK1	NTRK2	NTRK3	PAK3	PALB2	PARP1	PAX5
PAX8	PBRM1	PDCD1	PDCD1LG2	PDGFRA	PDGFRB	PDIA3	PGF	PHOX2B*	PIK3C2B	PIK3C2G	PIK3C3
PIK3CA	PIK3CB	PIK3CD	PIK3CG	PIK3R1	PIK3R2	PIK3R3	PIM1	PMS1	PMS2	POLB	POLD1
POLE	PPARG	PPP2R1A	PRDM1	PRKAR1A	PRKCA	PRKCB	PRKCG	PRKCI	PRKCQ	PRKDC	PRKN
PSMB8	PSMB9	PSME1	PSME2	PSME3	PTCH1	PTEN	PTGS2	PTPN11	PTPRD	PTPRT	RAC1
RAD50	RAD51	RAD51B	RAD51C	RAD51D	RAD52	RAD54L	RAF1	RARA	RB1	RBM10	RECQL4
REL	RET	RHOA	RICTOR	RNF43	ROS1	RPPH1	RPTOR	RUNX1	RUNX1T1	RXRA	SDHA
SDHB	SDHC	SDHD	SERPINB3	SERPINB4	SETD2	SF3B1	SGK1	SH2D1A*	SLC19A1*	SLC22A2*	SLC1B1*
SLCO1B3*	SMAD2	SMAD3	SMAD4	SMARCA4	SMARCB1	SMO	SOC1*	SOX2*	SOX9	SPEN	SPOP
SRC	STAG2	STAT3	STK11	SUFU	SYK	SYNE1	TAF1	TAP1	TAP2	TAPBP	TBX3
TEK	TERT	TET1	TET2	TGFBR2	TMSB4X*	TNF	TNFAIP3	TNFRSF14	TNFSF11	TOP1	TP53
TPMT*	TSC1	TSC2	TSHR	TYMS	U2AF1	UBE2A*	UBE2K	UBR5	UGT1A1*	USH2A	VDR*
VEGFA	VEGFB	VHL	WT1	XIAP	XPO1	XRCC2	ZNF217				

*Analysis of copy number alterations NOT available.

FUSION

ALK	BRAF	EGFR	FGFR1	FGFR2	FGFR3	MET	NRG1	NTRK1	NTRK2	NTRK3	RET	ROS1
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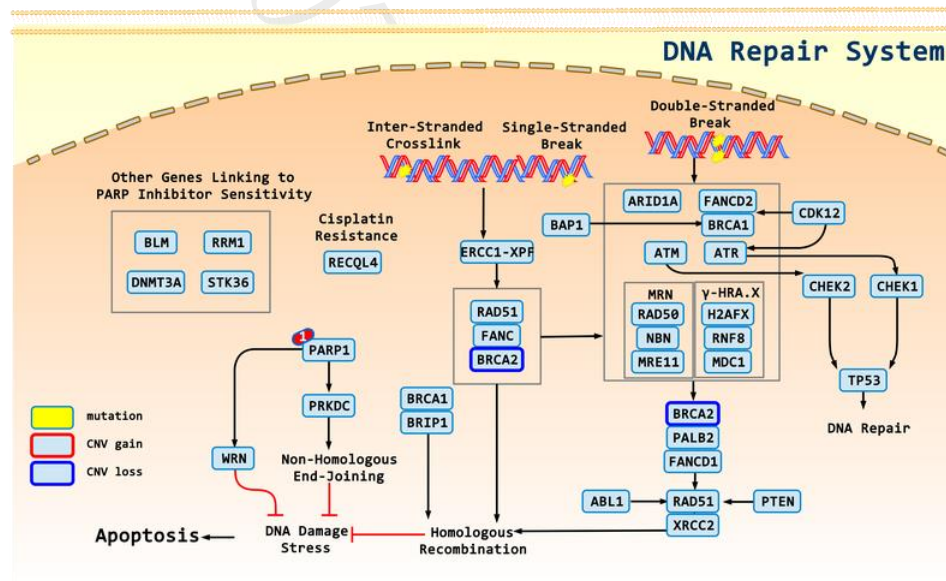
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APPENDIX

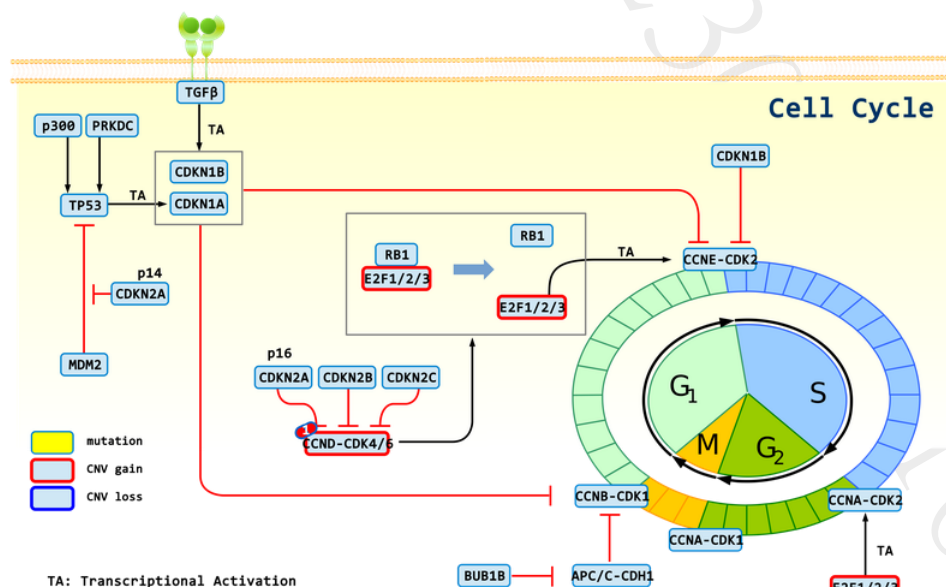
POSSIBLE THERAPEUTIC IMPLICATIONS FOR HETEROZYGOUS DELETION

Gene	Therapies	Possible effect
BRCA2	Niraparib, Olaparib, Rucaparib, Talazoparib	sensitive

SIGNALING PATHWAYS AND MOLECULAR-TARGETED AGENTS



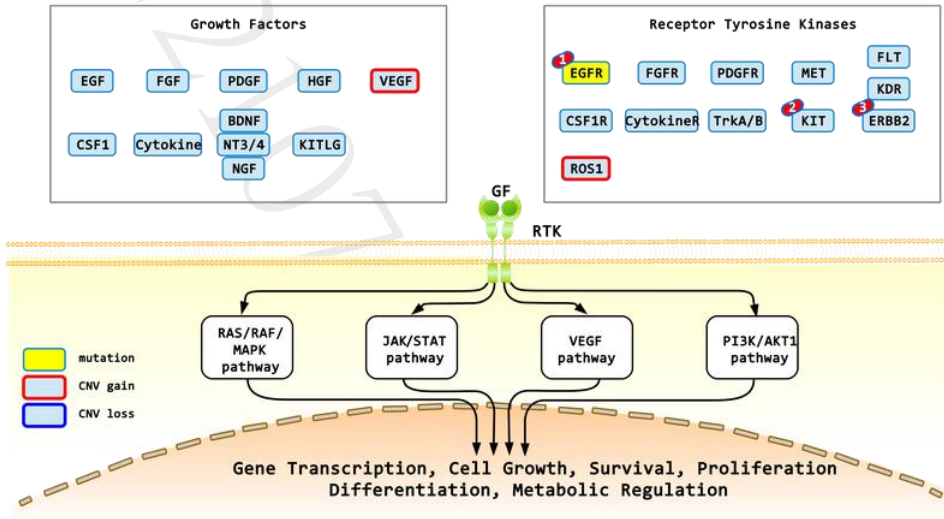
1: Olaparib, Niraparib, Rucaparib, Talazoparib



1: Abemaciclib

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Receptor Tyrosine Kinase/Growth Factor Signalling



1: Gefitinib, Afatinib, Erlotinib, Osimertinib, Dacomitinib; 2: Sorafenib; 3: Afatinib

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DISCLAIMER

法律聲明

本檢驗報告僅提供專業醫療參考，結果需經專業醫師解釋及判讀。基因突變資訊非必具備藥物或治療有效性指標，反之亦然。本檢驗報告提供之用藥指引不聲明或保證其臨床有效性，反之亦然。本基因檢測方法係由本公司研究開發，已經過有效性測試。

本檢驗報告非經本公司許可，不得私自變造、塗改，或以任何方式作為廣告及其他宣傳之用途。

本公司於提供檢驗報告後，即已完成本次契約義務，後續之報告解釋、判讀及用藥、治療，應自行尋求相關專業醫師協助，若需將報告移件其他醫師，本人應取得該醫師同意並填寫移件申請書，主動告知行動基因，行動基因僅能配合該醫師意願與時間提供醫師解說。

醫療決策需由醫師決定

任何治療與用藥需經由醫師在考慮病患所有健康狀況相關資訊包含健檢、其他檢測報告和病患意願後，依照該地區醫療照護標準由醫師獨立判斷。醫師不應僅依據單一報告結果(例如本檢測或本報告書內容)做決策。

基因突變與用藥資訊並非依照有效性排序

本報告中列出之生物標記變異與藥物資訊並非依照潛在治療有效性排序。

證據等級

藥物潛在臨床效益(或缺乏潛在臨床效益)的實證證據是依據至少一篇臨床療效個案報告或臨床前試驗做為評估。本公司盡力提供適時及準確之資料，但由於醫學科技之發展日新月異，本公司不就本報告提供的資料是否為準確、適宜或最新作保證。

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