

ACT Onco[®] + Report

| PATIENT | | |
|-----------------------------|--------------------------|----------------------|
| Identifier: 陳靖育 | | Patient ID: 48387822 |
| Date of Birth: Dec 09, 1977 | | Gender: Female |
| Diagnosis: Stomach cancer | | |
| ORDERING PHYSICIAN | | |
| Name: 陳明晃醫師 | | Tel: 886-228712121 |
| Facility: 臺北榮總 | | |
| Address: 臺北市北投區石牌路二段 201 號 | | |
| SPECIMEN | | |
| Specimen ID: S11124415E | Collection site: Stomach | Type: FFPE tissue |
| Date received: Jul 28, 2023 | Lab ID: AA-23-04941 | 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 | |
| Not detected | | | |

VARIANTS/BIOMARKERS WITH POTENTIAL CLINICAL SIGNIFICANCE

| Genomic Alterations/Biomarkers | Possibly Sensitive | Possibly Resistant |
|--------------------------------|---|--------------------|
| ARID1A Q611fs | Dasatinib, Olaparib, Rucaparib, Talazoparib | - |

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 |
|--------|-------------------|------------------|
| ARID1A | Q611fs | 7.3% |

- Copy Number Alterations

| Chromosome | Gene | Variation | Copy Number |
|--------------|------|-----------|-------------|
| Not detected | | | |

- 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) | 3.2 muts/Mb |
| Microsatellite Instability (MSI) | Microsatellite stable (MSS) |

Note:

- Loss of heterozygosity (LOH) information was used to infer tumor cellularity. Copy number alteration in the tumor was determined based on 30% tumor purity.
- 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 3B | | |
| ARID1A Q611fs | Olaparib | sensitive |
| Level 4 | | |
| ARID1A Q611fs | Dasatinib, Rucaparib, Talazoparib | 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 |
|---------------------|----------------------------|
| Not detected | |

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

| Genomic Alterations | Therapies | Effect | Level of Evidence | Cancer Type |
|-------------------------|-------------------------|-----------------------|-------------------|----------------|
| ARID1A Q611fs | Platinum-based regimens | Less sensitive | Clinical | Ovarian cancer |

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

ARID1A Q611fs

Biological Impact

The AT-rich interactive domain 1A (ARID1A) gene encodes the BAF250A protein, a component of the SWI/SNF chromatin remodeling complex that plays a role in various cellular functions, including DNA repair, DNA synthesis, and transcription^{[1][2]}. Haploinsufficiency of ARID1A is associated with tumor formation in some cancers^[3]. Inactivation of ARID1A is commonly observed in ovarian, endometrial, uterine, and, gastric cancers^{[4][5][6][7][8]}.

Q611fs mutation results in a change in the amino acid sequence beginning at 611, likely to cause premature truncation of the functional ARID1A protein (UniProtKB). This mutation is predicted to lead to a loss of ARID1A protein function, despite not being characterized in the literature.

Therapeutic and prognostic relevance

ARID1A is the most frequently mutated genes in ovarian clear cell carcinoma and several synthetic lethality hypothesis-based therapeutic targets in ARID1A mutated cancer are in development. For examples, 1) EZH2 inhibitor^{[9][10]}; 2) AKT-inhibitors MK-2206 and perifosine, as well as PI3K-inhibitor buparlisib^[11]; 3) multiple kinase inhibitor, dasatinib^[12].

Some preclinical evidences suggested that reduced ARID1A expression confers resistance to several HER2/PI3K/mTOR signaling cascade inhibitors such as AZD8055 and trastuzumab, through activation of annexin A1 expression^[13]. Loss or decreased expression of ARID1A has been reported to associate with resistance to platinum-based chemotherapies, shorter overall survival and lower complete response rate in ovarian cancer patients^{[14][15]}.

Low expression of ARID1A is a significant and independent prognostic factor for poor disease-free and overall survival in breast cancer patients^{[16][17]}. Besides, loss of ARID1A expression was more frequently seen in mismatch repair (MMR)-deficient colorectal cancers, predominantly in tumor with MLH1 promoter hypermethylation^[18]. Positive ARID1A expression could independently predict worse overall survival in stage IV CRC patients compared with negative ARID1A expression^[19].

ARID1A mutation has been determined as an inclusion criterion for the trials evaluating olaparib efficacy in metastatic biliary tract cancer (NCT04042831), and niraparib efficacy in melanoma (NCT03925350), pancreatic cancer (NCT03553004), or any malignancy, except prostate cancer (NCT03207347).

The preclinical study discovered that ARID1A deficiency sensitized some tumors to PARP inhibitor drugs, such as olaparib, rucaparib, talazoparib, and veliparib, which block DNA damage repair pathways^[20].

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US FDA-APPROVED DRUG(S)

Dasatinib (SPRYCEL)

Dasatinib is an oral Bcr-Abl tyrosine kinase inhibitor (inhibits the "Philadelphia chromosome") and Src family tyrosine kinase inhibitor. Dasatinib is produced by Bristol-Myers Squibb and sold under the trade name SPRYCEL.

- FDA Approval Summary of Dasatinib (SPRYCEL)

| | |
|---|---|
| DASISION ^[21] NCT00481247 | Chronic myeloid leukemia (Approved on 2010/10/28) |
| | - Dasatinib vs. Imatinib [ORR(%): 76.8 vs. 66.2] |
| [22] NCT00123474 | Chronic myeloid leukemia (Approved on 2007/11/08) |
| | - Dasatinib [ORR(%): 63.0] |
| [23] NCT00123487 | Acute lymphocytic leukemia (Approved on 2006/06/28) |
| | - Dasatinib [ORR(%): 38.0] |

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 ^[24] 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 ^[25] NCT02477644 | Ovarian cancer (Approved on 2020/05/08) |
| | HRD+ Olaparib + bevacizumab vs. Placebo + bevacizumab [PFS(M): 37.2 vs. 17.7] |
| POLO ^[26] 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 ^[27] 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 ^[28] NCT02000622 | Breast cancer (Approved on 2018/02/06) |
| | HER2-/gBRCA mutation Olaparib vs. Chemotherapy [PFS(M): 7 vs. 4.2] |

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| | |
|--|--|
| SOLO-2/ENGOT-Ov21 ^[29] 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 ^[30] NCT00753545 | Ovarian cancer, Fallopian tube cancer, Peritoneal carcinoma (Approved on 2017/08/17) |
| | - |
| | Olaparib vs. Placebo [PFS(M): 8.4 vs. 4.8] |

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 ^[31] 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] |

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 ^[32] 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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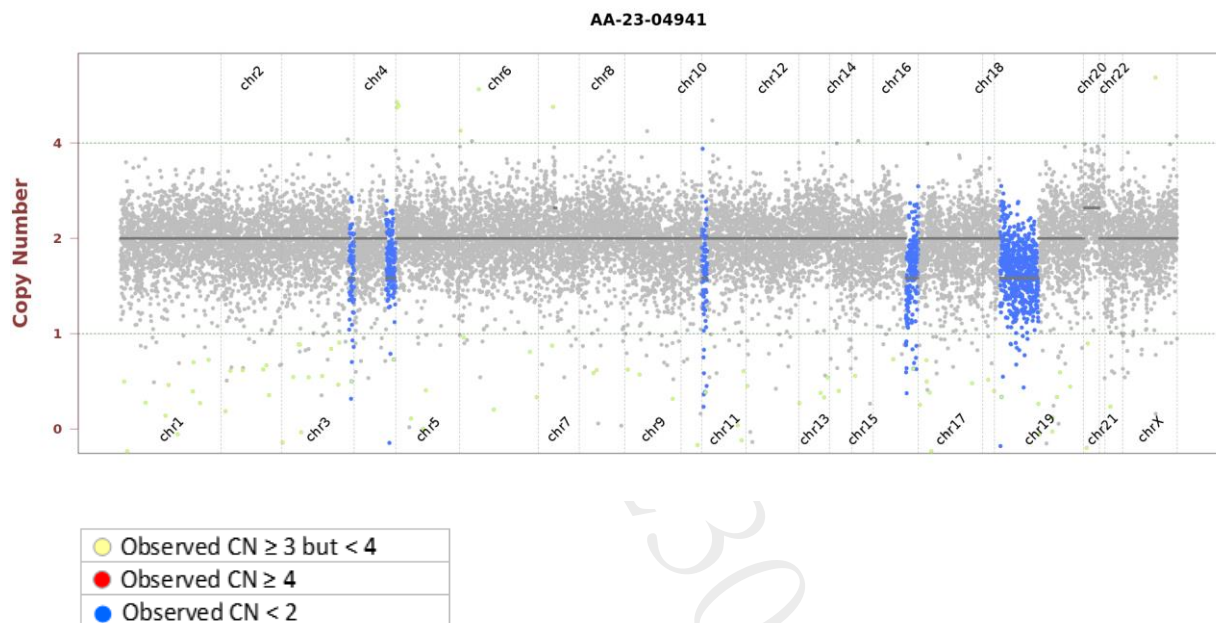
SUPPLEMENTARY INFORMATION OF TESTING RESULTS DETAILED INFORMATION OF VARIANTS WITH CLINICAL RELEVANCE

- Single Nucleotide and Small InDel Variants

| Gene | Amino Acid Change | Exon | cDNA Change | Accession Number | COSMIC ID | Allele Frequency | Coverage |
|--------|-------------------|------|-------------|------------------|-----------|------------------|----------|
| ARID1A | Q611fs | 4 | c.1832del | NM_006015 | - | 7.3% | 970 |

- 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 |
|---------|-------------------|------|-------------------------|------------------|-------------|------------------|----------|
| ALK | R1360W | 28 | c.4078C>T | NM_004304 | - | 49.7% | 290 |
| ALK | W1366R | 28 | c.4096T>C | NM_004304 | - | 8.3% | 289 |
| AXIN2 | E198D | 2 | c.594A>T | NM_004655 | - | 50.4% | 369 |
| BAP1 | D11N | 1 | c.31G>A | NM_004656 | COSM2853502 | 11.3% | 480 |
| BRCA2 | K2729N | 18 | c.8187G>T | NM_000059 | COSM5021109 | 44.3% | 1021 |
| CCNB2 | V301G | 7 | c.902T>G | NM_004701 | - | 48.8% | 2069 |
| CREBBP | A2419V | 31 | c.7256C>T | NM_004380 | COSM6914370 | 55.4% | 811 |
| DTX1 | Splice region | - | c.1549-6_1549-5delinsTG | NM_004416 | - | 48.5% | 639 |
| FGFR4 | D297N | 7 | c.889G>A | NM_213647 | - | 7.8% | 308 |
| JAK1 | N226S | 7 | c.677A>G | NM_002227 | - | 51.8% | 735 |
| JAK2 | V392M | 9 | c.1174G>A | NM_004972 | COSM5979661 | 45.2% | 991 |
| LIG1 | A293S | 11 | c.877G>T | NM_000234 | - | 54.2% | 522 |
| MSH6 | E1163V | 6 | c.3488A>T | NM_000179 | COSM4416035 | 48.8% | 1182 |
| MTOR | T588M | 11 | c.1763C>T | NM_004958 | COSM2119818 | 9.2% | 761 |
| MUC16 | S8808R | 3 | c.26422A>C | NM_024690 | COSM7377936 | 7.0% | 604 |
| NF1 | K2224R | 44 | c.6671A>G | NM_001042492 | - | 52.4% | 1276 |
| PIK3C2B | C691W | 14 | c.2073C>G | NM_002646 | COSM5749128 | 54.5% | 519 |
| PMS2 | D298G | 8 | c.893A>G | NM_000535 | - | 56.3% | 831 |
| PTCH1 | R1338H | 23 | c.4013G>A | NM_000264 | COSM2733116 | 49.1% | 53 |
| SDHA | I247V | 6 | c.739A>G | NM_004168 | - | 55.6% | 795 |
| TSHR | F525S | 10 | c.1574T>C | NM_000369 | - | 43.8% | 626 |

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: Jun 28, 2022
- Facility retrieved: 臺北榮總
- H&E-stained section No.: S11124415E
- Collection site: Stomach
- Examined by: Dr. Yun-An Chen
 1. The percentage of viable tumor cells in total cells in the whole slide (%): 25%
 2. The percentage of viable tumor cells in total cells in the encircled areas in the whole slide (%): 45%
 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: 783x
- Target Base Coverage at 100x: 95%

RNA test

- Average unique RNA Start Sites per control GSP2: 99

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.

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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).

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.

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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:

醫檢師陳韻鈺 博士
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檢字第 015647 號

Yun Yu Chen

Sign Off

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

Yeh

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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 | HRA5* | 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* | SLC18A1* |
| SLC18A1* | SMAD2 | SMAD3 | SMAD4 | SMARCA4 | SMARCB1 | SMO | SOCS1* | 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 |
|-----|------|------|-------|-------|-------|-----|------|-------|-------|-------|-----|------|

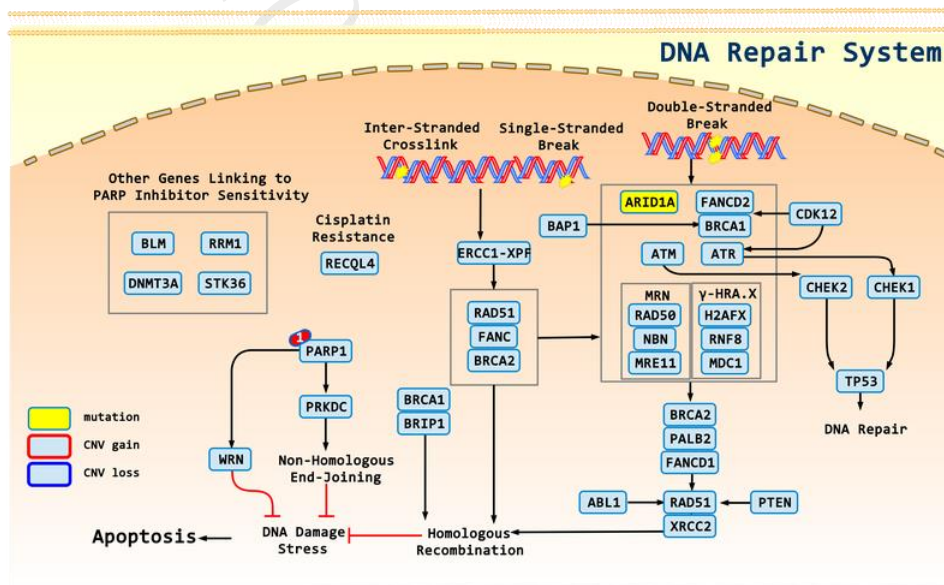
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APPENDIX

POSSIBLE THERAPEUTIC IMPLICATIONS FOR HETEROZYGOUS DELETION

Not Applicable.

SIGNALING PATHWAYS AND MOLECULAR-TARGETED AGENTS



1: Olaparib, Rucaparib, Talazoparib

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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。

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醫療決策需由醫師決定

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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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