



**Aegle Omics**  
Sequencing & Application

From Diagnosis to Therapy,  
we Prioritize Accuracy.



Dear Colleagues,

As you know, most non-communicable diseases stem from a combination of genetic factors, lifestyle choices, and environmental influences. Testing for gene mutations associated with cancer can help assess the risk of developing or passing on the disease. We're seeing a shift from cancer susceptibility gene panels to gene panels used in cancer treatment. As cancer physicians, we're pushed to go beyond conventional treatments, focusing on genomic-based approaches. This allows for personalized treatment plans, omitting ineffective or harmful therapies.

Through 'AEGLE OMICS,' we're committed to offering continuous support to oncologists in Sri Lanka, providing high-quality, precise testing. We've partnered with top-tier testing labs worldwide, ensuring access to comprehensive repositories. Our goal is to deliver valued services to leading health and research institutions globally. Our gene panels cover various cancers, facilitating quicker, easier clinical decisions without compromising professional integrity. Thank you for your interest in Precision Oncology.

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**Chairman** - AEGLE OMICS PVT LTD.

**Consultant** - Clinical Oncology & Radiotherapy.

**Principal Investigator** - Clinical Trials, Past President - Sri Lanka College of Oncologists.

**Ex Chairman** - Board of Oncolog, Sri Lanka

| New Test Code | Unique Test Name                                     | Genes/Biomarkers   | Test Category      | Sample Type                                      | Method | TAT     |
|---------------|--|--|--------------------|--|--------|---------|
| SLS161000     | Germline BRCA1 & BRCA2 test                          | BRCA 1, BRCA 2   | Germline           | Blood/ DBS EDTA Vacutainer (Purple Top)/ DBS Kit | NGS    | 21 Days |
| SLS161001     | Germline 3 Gene panel                                | BRCA1, BRCA2, TP53   | Germline           | Blood/ DBS EDTA Vacutainer (Purple Top)/ DBS Kit | NGS    | 21 Days |
| SLS161003     | HBOC Comprehensive Panel (19 Gene)                   | ATM, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MLH1, MSH2, MSH6, NBN, NF1, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, TP53   | Germline           | Blood/ DBS EDTA Vacutainer (Purple Top)/ DBS Kit | NGS    | 21 Days |
| SLS161004     | Lynch Syndrome panel                                 | EPCAM, MLH1, MSH2, MSH6, PMS2  | Germline           | Blood/ DBS EDTA Vacutainer (Purple Top)/ DBS Kit | NGS    | 21 Days |
| SLS161013     | Hereditary Cancer Test                               | APC, ATM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MAX, MEN1, MLH1, MSH2, MSH6, MUTYH, NF1, NF2, PALB2, PMS2, PTEN, RAD51C, RAD51D, RB1, RET, SDHAF2, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, TSC1, TSC2, VHL, WT1 | Germline           | Blood/ DBS EDTA Vacutainer (Purple Top)/ DBS Kit | NGS    | 21 Days |
| SLS162800     | Germline Homologous Recombination Repair Test (gHRR) | ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L   | Germline           | Blood/ DBS                                       | NGS    | 21 Days |
| SLS810011     | Final Diagnosis Panel                                | Sequential   | Somatic Speciality | FFPE Plastic container                           | IHC    | 5 Days  |
| SLS810001     | PDL-1 22C3 (Dako)                                    | PDL-1 22C3   | Somatic Speciality | FFPE Plastic container                           | IHC    | 5 Days  |
| SLS810004     | PDL-1 SP142 (Ventana)                                | PDL-1 SP142  | Somatic Speciality | FFPE Plastic container                           | IHC    | 5 Days  |

| New Test Code | Unique Test Name                                    | Genes/Biomarkers  | Test Category        | Sample Type                                      | Method   | TAT     |
|---------------|---|---|----------------------|--|----------|---------|
| SLS810006     | PDL-1 SP263 (Ventana)                               | PDL-1 SP263   | Somatic Speciality   | FFPE Plastic container                           | IHC      | 5 Days  |
| SLS140010     | EGFR Tissue   | Mutation detection EGFR (exon 18,19,20,21) including T790M  | Somatic Speciality   | FFPE Plastic container                           | RT PCR   | 10 Days |
| SLS150001     | MST (Sanger Sequencing)                             |   | Somatic Speciality   | Blood/ DBS EDTA Vacutainer (Purple Top)/ DBS Kit | Sanger   | 9 Days  |
| SLS140014     | MLPA BRCA1  | BRCA1   | Somatic Speciality   | Blood/ DBS EDTA Vacutainer (Purple Top)/ DBS Kit | Sanger   | 14 Days |
| SLS140015     | MLPA BRCA2  | BRCA2   | Somatic Speciality   | Blood/ DBS EDTA Vacutainer (Purple Top)/ DBS Kit | Sanger   | 14 Days |
| SLS162200     | Somatic BRCA Test                                   | BRCA1, BRCA2  | Somatic Small Panels | FFPE Plastic container                           | NGS      | 21 Days |
| SLS162800     | Somatic Homologous Recombination Repair Test (sHRR) | ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L  | Somatic Small Panels | FFPE Plastic container                           | NGS      | 21 Days |
| SLS162201     | Homologous Recombination Deficiency Test (HRD)      | BRCA1, BRCA2 and Genomic Scar Score (GSS)   | Somatic Small Panels | FFPE Plastic container                           | NGS      | 21 Days |
| SLS162400     | Lung Cancer Essential Panel                         | DNA genes (SNV, indels, CNV) - ALK, BRAF, EGFR, ERBB2, KRAS, MET, ROS1<br>RNA genes (fusions) - ALK, MET (exon 14 skipping), RET, ROS1                      | Somatic Small Panels | FFPE Plastic container                           | NGS      | 21 Days |
| SLS160001     | Lung Cancer Actionable Panel                        | DNA genes (SNV, indels, CNV) - ALK, BRAF, EGFR, ERBB2, KRAS, MET, ROS1<br>RNA genes (fusions) - ALK, MET (exon 14 skipping), RET, ROS1<br>PDL-1 22C3 (Dako) | Somatic Small Panels | FFPE Plastic container                           | NGS, IHC | 21 Days |

| New Test Code | Unique Test Name                      | Genes/Biomarkers  | Test Category        | Sample Type   | Method   | TAT     |
|---------------|---------------------------------------|---|----------------------|---|----------|---------|
| SLS160002     | Lung Cancer Comprehensive Panel       | DNA genes (SNV, indel, CNV) - ALK, BRAF, EGFR, ERBB2, KEAP1, KRAS, MET, MAP2K1, NRAS, PIK3CA, PTEN, ROS1, STK11, TP53<br>RNA genes (fusions) - ALK, MET (exon 14 skipping), NTRK1, NTRK2, NTRK3, RET, ROS1<br>PDL-1 22C3 (Dako) | Somatic Small Panels | FFPE Plastic container  | NGS, IHC | 21 Days |
| SLS140006     | EGFR liquid biopsy                    | EGFR,T790M (EGFR L858R and Del 19)  | Somatic Marker       | Whole Blood in Streck Tubes<br>Streck tube                    | PCR      | 21 Days |
| SLS162600     | Colorectal Cancer Essential Panel     | BRAF, ERBB2, KRAS, MET,NRAS, PIK3CA, PTEN   | Somatic Small Panels | FFPE Plastic container  | NGS      | 21 Days |
| SLS160003     | Colorectal Cancer Actionable Panel    | BRAF, ERBB2, KRAS, MET,NRAS, PIK3CA, PTEN<br>MSI by PCR   | Somatic Small Panels | FFPE & Blood Plastic container & EDTA Vacutainer (Purple Top) | NGS, PCR | 21 Days |
| SLS160004     | Colorectal Cancer Comprehensive Panel | AKT1, APC, BRAF, CTN-NB1, DDR2, EGFR, ERBB2, ERBB3, FBXW7, KRAS, MAP2K1, MET, MLH1, MSH2, MSH6, NOTCH1, NRAS, PIK3CA, PMS2, PTEN, SMAD4, TP53<br>MSI by PCR   | Somatic Small Panels | FFPE & Blood Plastic container & EDTA Vacutainer (Purple Top) | NGS, PCR | 21 Days |
| SLS162900     | Endometrial Cancer Test               | MMRD mutations, POLE mutations, TP53  | Somatic Small Panels | FFPE Plastic container  | NGS      | 21 Days |
| SLS163000     | Thyroid cancer basic panel            | ALK, BRAFV600E, NTRK, PIK3CA, RAS, RET  | Somatic Small Panels | FFPE Plastic container  | NGS      | 21 Days |
| SLS163001     | Thyroid cancer advance panel          | DNA Genes (SNV, Indels, CNV) ALK, BRAFV600E, NTRK ,PIK3CA, RAS, RET, RNA genes (fusions) - ALK, RET, NTRK   | Somatic Small Panels | FFPE Plastic container  | NGS      | 21 Days |

| New Test Code | Unique Test Name  | Genes/Biomarkers   | Test Category                         | Sample Type            | Method | TAT     |
|---------------|---|--|---------------------------------------|------------------------|--------|---------|
| SLS162000     | Somatic Advantage 74 Gene Test  | DNA genes: AKT1, ALK, APC, AR, ARID1A, ATM, ATR, BAP1, BARD1, BRAF, BRCA1, BRCA2, BRIP1, CDK12, CDKN2A, CHEK1, CHEK2, CTNNB1, DDR2, EGFR, ERBB2, ERBB3, ESR1, EZH2, FANCA, FANCL, FBXW7, FGFR1, FGFR2, FGFR3, HRAS, IDH1, IDH2, KEAP1, KIT, KRAS, MAP2K1, MAP2K2, MET, MLH1, MRE11, MSH2, MSH6, NBN, NF1, NOTCH1, NRAS, NTRK1, NTRK2, NTRK3, PALB2, PBRM1, PDGFRA, PIK3CA, PMS2, POLE, PTCH1, PTEN, RAD51B, RAD51C, RAD51D, RAD54L, RET, ROS1, SMAD4, SMO, STK11, TERT, TP53<br>RNA genes: ALK, BRAF, ERG, EWSR1, FGFR2, FGFR3, FUS, NRG1, NTRK1, NTRK2, NTRK3, PPARG, RET, ROS1<br>MSI by NGS | Comprehensive Genomic Profiling (CGP) | FFPE Plastic container | NGS    | 18 Days |
| SLS162001     | Liquid Biopsy 56 Gene Panel (Ct DNA)                                      | ABL1, AKT1, ALK, APC, ATM, BRAF, CDH1, CDKN2A, CSF1R, CTNNB1, DDR2, DNMT3A, EGFR, ERBB2, ERBB4, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, FLT3, FOXL2, GNA11, GNAQ, GNAS, HNF1A, HRAS, IDH1, IDH2, JAK2, JAK3, KDR, KIT, KRAS, MAP2k1, MET, MLH1, MPL, MSH6, NOTCH1, NPM1, NRAS, PDGFRA, PIK3CA, PTEN, PTPN11, RB1, RET, SMAD4, SMARCB1, SMO, SRC, STK11, TP53, TSC1, VHL  | Comprehensive Genomic Profiling (CGP) | Blood Streck tube      | NGS    | 21 Days |
| SLS162002     | Comprehensive Genomic Profiling - Strand Advantage 500 Basic (DNA)        | 523 Genes, Tumour Mutation Burden (TMB), Microsatellite Instability (MSI)  | Comprehensive Genomic Profiling (CGP) | FFPE Plastic container | NGS    | 21 Days |
| SLS162003     | Comprehensive Genomic Profiling - Strand Advantage 500 Advanced (DNA+RNA) | 523 Genes, 55 Fusion, Tumour Mutation Burden (TMB), Microsatellite Instability (MSI)   | Comprehensive Genomic Profiling (CGP) | FFPE Plastic container | NGS    | 21 Days |

# BREAST CANCER

## BREAST – RISK SCREENING & PREDICTIVE VALUES

| Test Code | Test Name                             | Sample Requirement                                    | TAT     | Special Instruction                             |
|-----------|---------------------------------------|---|---------|---|
| NA1030    | BRCA1 and BRCA2 Gene Sequencing Panel | 3-4 mL Peripheral Blood in 1 Lavender Top (EDTA) tube | 15 Days | History Biopsy & ER/PR Her2neu report mandatory |

Identifies Mutations in 1/2 genes leading to hereditary breast cancer. Detects point mutations in the sequence and small indel mutations

| Test Code | Test Name                                     | Sample Requirement  | TAT     | Special Instruction                                       |
|-----------|---|---|---------|---|
| NA2452    | BRCA1 and BRCA2 Somatic Gene Sequencing Panel | FFP embeded tissue block or at least 10 section of Formalin fixed paraffin embedded tissue block of thickness 5-10µm with marked area of enriched tumor and accompanying pathology report | 15 Days | Clinical history, Biopsy & ER/PR Her2neu report mandatory |

For Somatic Breast Cancer Cases

| Test Code | Test Name   | Sample Requirement                            | TAT    | Special Instruction   | Clinical Utility                                  |
|-----------|-------------|---|--------|---|---|
| IA1892    | GCDFP-15    | Formalin fixed paraffin embedded tissue block | 4 Days | Clinical History, Histopathology Report, Any Radiological Findings required | Diagnosis of breast cancer metastasis             |
| IA1868    | Mammaglobin | FFP embedded tissue block                     |        | Clinical History, Histopathology Report, Any Radiological Findings required | Diagnosis of PRIMARY AND breast cancer metastasis |

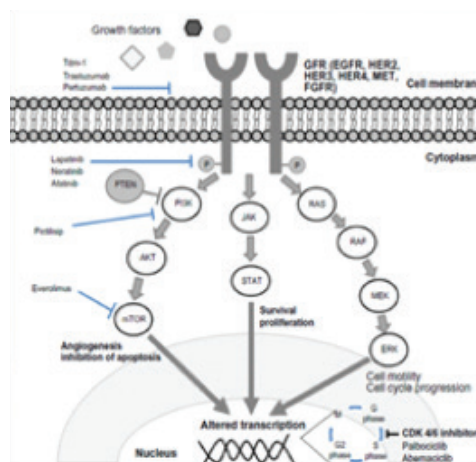
| Test Code | Test Name | Sample Requirement                | TAT | Special Instruction                              |
|-----------|-----------|-----------------------------------|-----|--|
| AO2904    | CA 27.29  | 2 mL (1 mL min.) Serum from 1 SST |     | Sample by 6th of the month, report after 3 weeks |
| AO1175    | CA 15.3   | 2 mL (1 mL min.) Serum from 1 SST |     | SERUM  |

Monitor the response to therapy and if elevated suggests recurrence in women with Stage II or III breast Cancer.

The analysis of actionable targets in breast cancer involves several approaches, including:

- Tumor biopsy or surgical specimen:** A tissue sample is collected from the breast tumor through a biopsy or during surgery. This sample is then analyzed to determine the molecular characteristics of the tumor, including hormone receptor status (ER, PR), HER2 expression, and genetic mutations.
- Immunohistochemistry (IHC):** IHC is a technique that uses antibodies to detect specific proteins in the tumor tissue. It can be used to determine the expression levels of hormone receptors (ER, PR) and HER2 protein.
- Fluorescence in situ hybridization (FISH):** FISH is a molecular technique that can determine the amplification of the HER2 gene. It involves using fluorescently labeled DNA probes that bind to specific regions of the HER2 gene. This technique helps identify HER2-positive breast cancer cases.
- Next-generation sequencing (NGS):** NGS is a high-throughput sequencing technology that can analyze multiple genes simultaneously. It can identify genetic mutations and alterations in breast cancer-related genes, such as BRCA1, BRCA2, PIK3CA, and others. NGS can also be used to identify potential therapeutic targets and predict response to targeted therapies.

5. **Gene expression profiling: (GEP)** Techniques like microarray analysis or RNA sequencing can measure the expression levels of thousands of genes in the tumor tissue. This can provide insights into the molecular subtype of breast cancer (e.g., luminal A, luminal B, HER2-enriched, basal-like), which can guide treatment decisions.



The analysis of actionable targets in breast cancer is typically performed by a multidisciplinary team of pathologists, oncologists, and molecular biologists, who interpret the results and guide treatment decisions based on the specific characteristics of the tumor. There are several genomic targetable anti-cancer drugs used in the treatment of breast cancer. These drugs target specific genetic mutations or alterations in cancer cells. Some of the commonly used genomic targetable drugs for breast cancer include:

1. **HER2-Targeted Therapy:** Drugs like trastuzumab, pertuzumab, ado-trastuzumab emtansine (T-DM1), and neratinib specifically target the HER2 protein, which is overexpressed in HER2-positive breast cancers.
2. **CDK4/6 Inhibitors:** Cyclin-dependent kinase 4/6 inhibitors, such as palbociclib, ribociclib, and abemaciclib, target the CDK4/6 pathway, which is frequently dysregulated in breast cancer.
3. **PARP Inhibitors:** Poly (ADP-ribose) polymerase (PARP) inhibitors, such as olaparib and talazoparib, target cancers with BRCA1 or BRCA2 mutations, which are involved in DNA repair.
4. **PI3K Inhibitors:** Phosphatidylinositol 3-kinase (PI3K) inhibitors, like alpelisib, target the PI3K pathway, which is commonly altered in breast cancer.
5. **AKT Inhibitors:** AKT inhibitors, such as capivasertib, target the AKT pathway, which is involved in cell growth and survival.
6. **FGFR Inhibitors:** Fibroblast growth factor receptor (FGFR) inhibitors, like erdafitinib, target cancers with FGFR alterations, which are involved in cell signaling and growth.

#### Role of ctDNA in Breast Cancer

Marta Sant, Adrià Bernat-Peguera, [...], and Mireia Margelí

TP53, PIK3CA, ESR1, GATA3, ARID1A and PTEN are the most frequently altered. These mutations can be truncal, when they are found in all the patient's cancer cells, or subclonal, when they are randomly dispersed throughout the genome. The ctDNA dynamics of subclonal mutations have a limited potential to predict clinical outcome.

PIK3CA encodes for the p110a subunit of PI3K. PIK3CA mutations are associated with worse prognosis, although they confer sensitivity to PI3K inhibitors (PI3Ki) such as tasiselisib, alpelisib, buparlisib and copanlisib.

Although there are no validated predictive biomarkers of response to CDK 4/6 inhibitors, early ctDNA dynamics of PIK3CA truncal mutations predicted sensitivity to Palbociclib, a CDK 4/6 inhibitor. Palbociclib is a cytostatic drug, and its effects decrease PIK3CA-mutant ctDNA, indicating that ctDNA PIK3CA mutations may be useful as an early predictor of response, as was observed in the PALOMA-3 trial of ER-positive/HER2-negative advanced breast cancer patients who had previously progressed to endocrine therapy.



ESR1 encodes for an ER, and its mutations are found in 30% of patients receiving endocrine therapy. However, if a CDK 4/6 inhibitor is used together with Aromatase inhibitors, the ESR1 mutation rate decreases. ESR1 mutations are located in the ligand-binding domain and are hormone-independent activating mutations. In some cases, methylation of the ESR1 promoter causes gene silencing, leading to a lack of ER expression and resistance to endocrine therapy. Activating ESR1 mutations are acquired mutations and not a clonal selection, as they are not detected in primary breast cancer and they are found in the subclonal population.

Druggable target gene alterations detected in cDNA in metastatic breast cancer. \* (asterisk) means translation termination (stop) codon.

| Gene (Hot spot mutation)                        | Effect on Treatment Response  |
|---|---|
| PTEN<br>(R130Q, R130G, R130*, R130P, R130Qfs*4) | Sensitivity to capivasertib / ipatasertib (AKT inhibitors) + paclitaxel<br>Resistance to PI3Ki (loss of PTEN)               |
| PIK3CA<br>(H1047R, H1047L, N345K, E545K, ES42K) | Resistance to endocrine therapy (truncal mutations)<br>Sensitivity to PI3Ki (tasclisib, alpelisib, buparlisib, copanlisib). |
| ESR1<br>(Y537C, Y537N, Y537S, S463P, D538G)     | Resistance to endocrine therapy (subclonal mutation)  |
| AKT (E 17K)                                     | Sensitivity to capivasertib (AKT kinase inhibitor)  |
| HER2 (L755S, V777L)                             | HER2 inhibitor (bind to kinase domain) (lapatinib, neratinib)   |

[https://blog.lgcclinicaldiagnostics.com/bcr12?utm\\_campaign=CG\\_2023-10\\_Breast%20Cancer%20Awareness&utm\\_medium=email&\\_hsmi=279085006&\\_hsenc=p2ANqtz-\\_exT6gJSbNsVsEcg2sPZsKXcjNK5lOvBena0FaJ5Ml1s9-9LQqPqwhK1gDtMlWlaFQrG43HmIGJ2ltribpX00MqPFLPQ&utm\\_content=279085006&utm\\_source=hs\\_email](https://blog.lgcclinicaldiagnostics.com/bcr12?utm_campaign=CG_2023-10_Breast%20Cancer%20Awareness&utm_medium=email&_hsmi=279085006&_hsenc=p2ANqtz-_exT6gJSbNsVsEcg2sPZsKXcjNK5lOvBena0FaJ5Ml1s9-9LQqPqwhK1gDtMlWlaFQrG43HmIGJ2ltribpX00MqPFLPQ&utm_content=279085006&utm_source=hs_email)

| Test Code | Test Name                                     | Sample Requirement                                   | TAT     | Method  |
|-----------|---|--|---------|---|
| MC1276    | mammaCORE BRCA 1&2 Deletion/Duplication Panel | 3-4mL Peripheral Blood in 1 Lavender Top (EDTA) tube | 15 Days | Multiplex Ligation Dependent Probe Amplification (MLPA) |

Identifies mutations in 1/2 gene leading to hereditary breast cancer. Detects larger deletions or duplications of the entire regions of the gene.

| Test Code | Test Name                          | Components  | Sample Requirement                                     | TAT     | Method   |
|-----------|------------------------------------|---|--|---------|--|
| P00353    | mammaCORE BRCA Advanced Panel      | BRCA 1 & 2 Germline+ Somatic Mutation Analysis                    | 3-4 mL EDTA Whole Blood and FFP embedded tissue block  | 15 Days | Next Generation Sequencing   |
| P00354    | mammaCORE BRCA Advanced Plus Panel | BRCA 1 & 2 Germline+ Somatic Mutation Analysis + Del/Dup Analysis | EDTA Whole Blood and FFP embedded tissue block         | 15 Days | Multiplex Ligation Dependent Probe Amplification, Next generation Sequencing |
| NA1031    | mammaCORE BRCA Comprehensive Panel | BRCA 1 & 2 Germline+Del/Dup Analysis                              | 3-4 mL Peripheral Blood in 1 Lavender Top (EDTA) tube. | 30 Days | Next Generation Sequencing   |
| P00008    | mammaCORE PANEL 1                  | ER, PR, HER2/neu  | FFP embedded tissue block                              | 4 Days  | IHC  |
| P00009    | mammaCORE PANEL 2                  | ER, PR, HER2/neu, Ki67  | FFP embedded tissue block                              | 4 Days  | IHC  |

| Test Code | Test Name         | Components                  | Sample Requirement        | TAT    | Method |
|-----------|-------------------|-----------------------------|---------------------------|--------|--------|
| P00062    | mammaCORE Panel 3 | Ki-67, p53,ER/PR, Her2/ neu | FFP embedded tissue block | 4 Days | IHC    |
| IA1868    | Mammaglobin       |                             | FFP embedded tissue block | 4 Days | IHC    |

### Diagnosis, Prognosis and therapy indication for Breast cancer patients

| Test Code | Test Name                                    | Sample Requirement   | TAT     | Method                     | Shipping & Stability Conditions  |
|-----------|--|--|---------|----------------------------|--|
| P01065    | HRR Gene Panel (Somatic + Germline) Extended | Formalin fixed paraffin embedded tissue block + Peripheral Blood | 2 Weeks | Next Generation Sequencing | Tissue-Ambient (18-25°C) temperature. Do not Freeze. +Blood-Transport in 2 to 8°C (with cold pack) |
| P00397    | FUS-DDIT3                                    | FFPE+ Peripheral Blood   | 2 Weeks | Next Generation Sequencing | Ambient (18-25°C) temperature. Do not Freeze.  |

ATM, MRE11, BARD1, NBN, BRCA1, PALB2, BRCA2, PPP2R2A, BRIP1, RAD51B, CDK12, RAD54L, CHEK2, TP53 FANCD2, RAD51C, RAD51D

| Test Code | Test Name                 | Sample Requirement                     | TAT     | Method                     | Shipping & Stability Conditions               |
|-----------|---------------------------|--|---------|----------------------------|---|
| NA2579    | HRR Gene Panel (Germline) | 2ml Peripheral Blood (EDTA Vacutainer) | 2 Weeks | Next Generation Sequencing | Ambient (18-25°C) temperature. Do not Freeze. |

ATM, MRE11, BARD1, NBN, BRCA1, PALB2, BRCA2, PPP2R2A, BRIP1, RAD51B, CDK12, RAD54L, CHEK2, TP53 FANCD2, RAD51C, RAD51D

| Test Code | Test Name                          | Sample Requirement                     | TAT     | Method                     | Shipping & Stability Conditions        |
|-----------|------------------------------------|--|---------|----------------------------|--|
| NA3166    | HRR Gene Panel (Germline) Extended | 2ml Peripheral Blood (EDTA Vacutainer) | 2 Weeks | Next Generation Sequencing | Transport in 2 to 8°C (with cold pack) |

ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCD2, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD54L, TP53, CHEK1, FANCL, RAD50, RAD51, RAD51C, RAD51D, RAD52, XRCC2, KRAS, PIK3CA, POLD1, POLE, PTEN

| Test Code | Test Name                | Sample Requirement                            | TAT     | Method                     | Shipping & Stability Conditions               |
|-----------|--------------------------|---|---------|----------------------------|---|
| NA2577    | HRR Gene Panel (Somatic) | Formalin fixed paraffin embedded tissue block | 2 Weeks | Next Generation Sequencing | Ambient (18-25°C) temperature. Do not Freeze. |

ATM, MRE11, BARD1, NBN, BRCA1, PALB2, BRCA2, PPP2R2A, BRIP1, RAD51B, CDK12, RAD54L, CHEK2, TP53, FANCD2, RAD51C, RAD51D

| Test Code | Test Name                         | Sample Requirement                            | TAT     | Method                     | Shipping & Stability Conditions               |
|-----------|-----------------------------------|---|---------|----------------------------|---|
| NA3167    | HRR Gene Panel (Somatic) Extended | Formalin fixed paraffin embedded tissue block | 2 Weeks | Next Generation Sequencing | Ambient (18-25°C) temperature. Do not Freeze. |

ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCD2, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD54L, TP53, CHEK1, FANCL, RAD50, RAD51, RAD51C, RAD51D, RAD52, XRCC2, KRAS, PIK3CA, POLD1, POLE, PTEN

| Test Code | Test Name                          | Sample Requirement   | TAT     | Method                     | Shipping & Stability Conditions                      |
|-----------|------------------------------------|--|---------|----------------------------|--|
| NA3163    | HRR Somatic reflex to HRR Germline | Formalin fixed paraffin embedded tissue block + Peripheral Blood | 16 Days | Next Generation Sequencing | Tissue-Ambient (18-25°C) temperature. Do not Freeze. |

ATM, MRE11, BARD1, NBN, BRCA1, PALB2, BRCA2, PPP2R2A, BRIP1, RAD51B, CDK12, RAD54L, CHEK2, TP53 FANCD2, RAD51C, RAD51D

# COLORECTAL CA

Blockade of EGFR Over Expression with the monoclonal antibodies (mAbs) cetuximab or Panitumumab is effective in RAS wild-type CRC.

At relapse, the majority of patients develop RAS mutations, while a subset of patients acquires EGFR extracellular domain mutations. Overcoming RAS Mutations in mCRC (40%) Predicts a Negative response to EGFR inhibitors.

KRAS G12C mutation (found in 3% of mCRC) Sotorasib (AMG 510)

(HER2) amplifications is a negative predictive biomarker for anti-EGFR therapies. Found in ~3%-4% of patients with mCRC and in 6%-8% of patients with KRAS-wild-type mCRC.

BRAF V600E mutations occur in up to 12% of mCRCs and are nearly always mutually exclusive with KRAS mutations. This mutation is associated with worse prognosis and predicts a poorer response to anti-EGFR treatment.

Based on the similar OS rates for doublet and triplet combinations, Encorafenib/ Cetuximab is currently recommended in the chemotherapy- refractory setting of BRAF V600E-mutated mCRC.

HER2-positive mCRC; Number of Trastuzumab based treatments have been tried. (ie: T-DM1, Trastuzumab/Pertuzumab, Trastuzumab/ Lapatinib etc)

Trastuzumab Deruxtecan in HER2-positive mCRC, showed a meaningful improvement in terms of ORR, PFS and OS; 30% of these patients had previously received anti-HER2 treatment.

MSI and NTRK Fusions in mCRC.

MSI is found in 5% of mCRC and is a biomarker of response to immunotherapy in the metastatic setting. The anti-programmed cell death protein 1 (PD-1) agent Pembrolizumab has been tested in mCRC in several clinical trials. Across studies, the ORR was 40%.

NTRK fusions have been reported in 1.5% of mCRC patients. In mCRC, rearrangements in NTRK genes are more commonly detected in MSI-H tumours and wild-type BRAF/ KRAS/NRAS.

Larotrectinib and Entrectinib have produced dramatic and prolonged responses in gastrointestinal malignancies with NTRK fusions.

| Test Code | Test Name                                 | Sample Requirement   | TAT    | Method                              | Shipping & Stability Conditions                                    | Clinical Utility   |
|-----------|---|--|--------|-------------------------------------|--|--|
| P00005    | KRAS and NRAS Mutation Analysis           | Formalin fixed paraffin embedded tissue block                            | 5 Days | Real Time Polymerase Chain Reaction | Transport at ambient (18-25°C) temperature                         | This assay is useful for the detection of KRAS and NRAS mutations which are associated with shorter progression-free survival in Colorectal cancer.  |
| ME1068    | KRAS Somatic Mutation (Exon 2-4) Analysis | Formalin fixed paraffin embedded tissue block                            | 5 Days | Real Time Polymerase Chain Reaction | Transport at ambient (18-25°C) temperature                         | This assay is useful for the detection of KRAS mutations which are associated with shorter progression-free survival in Colorectal cancer. Codon 12 and codon 13 are more prevalent while codon 61,117,146 forms less than 1% of KRAS mutations. |
|           | DPD/DPYD mutation analysis                | 3-4 mL Bone marrow/ Peripheral Blood in Lavender Top (EDTA) vacutainers. | 5 Days | PCR, Sequencing                     | Transport in 2 to 8°C (with cold pack). Stable at 4°C for 72 hours | To confirm the clinical diagnosis of dihydropyrimidine dehydrogenase (DPD) deficiency in affected patients and for detection of IVS14+1G>A mutation in asymptomatic carriers   |

| Test Code | Test Name                 | Sample Requirement   | TAT     | Method    | Special Instructions   | Shipping & Stability Conditions             | Clinical Utility  |
|-----------|---------------------------|--|---------|-----------|--|---|---|
| P00006    | coloCORE Panel 1          | Formalin fixed paraffin embedded tissue block  | 7 Days  |           | Samples should reach the lab ASAP(2-4°C). If more than 72 hours then specimens should be frozen, preferably at -80°C, and ship in dry ice. | Transport at ambient (18-25°C) temperature  | This assay is useful for the detection of KRAS, NRAS and BRAF mutations which are associated with shorter progression-free survival in Colorectal cancer. |
| P00023    | coloCORE Panel 2          | Formalin fixed paraffin embedded tissue block  | 7 Days  | IHC / PCR | Clinical history is mandatory.   | Transport at ambient (18-25°C) temperature. |   |
| P00616    | coloCORE Targeted Panel-1 | Formalin-fixed paraffin-embedded tissue block, 3 mL Peripheral Blood in EDTA (Lavender Top) Tube | 15 Days | NGS / PCR |  |   |   |
| P00617    | coloCORE Targeted Panel-2 | Formalin fixed paraffin embedded tissue block  | 15 Days | NGS / IHC |  |   |   |
| ME1070    | BRAF                      |  | 5 Days  | RT / PCR  | Clinical history   | Transport at ambient (18-25°C) temperature  | Predict response to EGFR-targeted immunotherapy in patients with metastatic colorectal cancer   |
| IA1070    | BRAF V600E (VE1)          |  | 4 Days  | IHC       | Clinical history   | Transport at ambient (18-25°C) temperature  |   |
| IA1432    | CK19                      | FFP  | 4 Days  | IHC       | Clinical History, Histopathology Report, Any Radiological Findings required  | Transport at ambient (18-25°C) temperature  | Diagnosis of Pancreatic Cancer  |
| IA1435    | CK20                      | FFP  | 4 Days  | IHC       | Clinical History, Histopathology Report, Any Radiological Findings.  | Transport at ambient (18-25°C) temperature  | Diagnosis of Large Intestinal CA.   |

| Test Code | Test Name             | Sample Requirement  | TAT    | Method   | Special Instructions  | Shipping & Stability Conditions            | Clinical Utility  |
|-----------|-----------------------|---|--------|--|---|--|---|
| YB1060    | EGFR (FISH)           | Formalin fixed paraffin embedded tissue block   | 6 Days | IHC  | Clinical history mandatory.   | Transport at ambient (18-25°C) temperature | EGFR-targeted therapy in metastatic colorectal cancer cases.  |
| IA1060    | EGFR (IHC)            | FFPE block or submit tissue in 10% formal saline  | 5 Days | IHC  | Clinical history mandatory. Slides to be transported in proper slide mailers (plastic) with proper labelling. | Ambient                                    |   |
| MG1619    | EGFR T790M            | 1 Streck BCT/ Paxgene Tube with 9-9.5 mL blood. Do not fill till the end so as to avoid hemolysis | 5 Days | Droplet Digital Polymerase Chain Reaction                  | Previous EGFR report  | Stable at 4°C for 7 days                   | To Determine presence of Primary and Secondary EGFR Mutations |
| P00015    | EGFR (PCR), ALK (IHC) | Formalin fixed paraffin embedded tissue block   | 5 Days | Real Time Polymerase Chain Reaction & Immunohistochemistry | Clinical history mandatory.   | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC        |

## GASTROINTESTINAL STROMAL TUMORS

| Test Code | Test Name  | Sample Requirement | TAT     | Method | Shipping & Stability Conditions |                                       |
|-----------|--|--------------------|---------|--------|---------------------------------|---------------------------------------|
| MM1336    | PDGFRA Mutation Analysis (Solid Tumors)                | FFP                | 8 Days  | PCR    | Transport at ambient (18-25°C)  | PDGFRA confirm the diagnosis of GIST. |
| IA1006    | CD117/c-Kit (KIT Mutation in Exon 11, 9,13,17)         | FFP                | 5 Days  | IHC    | Transport at ambient (18-25°C)  | GIST stomach, small intestine,        |
| MM1006    | c-KIT Mutation analysis which looks at Exon 9,11,13,17 | FFP                | 10 Days | PCR    | Transport at ambient (18-25°C)  | GIST                                  |
| IA1794    | DOG 1  | FFP                | 5 Days  | IHC    | Transport at ambient (18-25°C)  | GIST diagnosis                        |

# LUNG CANCER

Key molecular targets include Epidermal Growth Factor Receptor (EGFR) mutation, Anaplastic Lymphoma Kinase (ALK) translocation and several relatively uncommon oncogenic drivers, while for patients without an oncogene driver, the key biomarker

is PD-L1 expression.

## Targeting the Uncommon Mutations:

The ambit of potentially targetable oncogenic drivers in NSCLC expanded in the 2010s, and, in addition to EGFR and ALK, there are seven others (listed alphabetically below). However, in contrast with EGFR/ALK, targeted drugs for these molecular subgroups have largely been evaluated/approved after phase I/II trials and in the relapse setting.

- BRAF mutations:** Dabrafenib+trametinib is approved for BRAF V600E mutation-positive NSCLC with similar ORRs (63%) in pretreated (mPFS, 9.7 months) and treatment-naïve (mPFS, 10.9 months) patients (NCT01336634). Vemurafenib (NCT01524978; NCT02304809) showed inferior efficacy.
- HER2 (ErbB2) mutations:** Trastuzumab deruxtecan (n=91, ORR 55%, mPFS 8.2 months; NCT02675829; under priority review by the FDA at the time of publication) and Pyrotinib (n=60, ORR 30%, mPFS 6.9 months; NCT03505710; available only in China) have shown 'promising' activity.
- KRAS G12C mutations:** Sotorasib (CodeBreak100[NCT03600883]), approved by the FDA and the EMA as a second-line therapy, is associated with an ORR of 32%, a mPFS of 6.3 months and OS of 12.4 months. Adagrasib (KRYSTAL-1 [NCT03785249]) has also received FDA 'breakthrough therapy designation'.
- MET exon 14 skipping:** Capmatinib (GEOMETRY Mono-1 [NCT02414139]) showed a higher ORR for treatment-naïve patients (68% versus 41% pretreated), while Tepotinib responses (VISION [NCT02864992]) were similar (44% treatment-naïve, 48% pre-treated) for MET exon 14 'skipping' mutations.
- NTRK (Neurotrophic tyrosine receptor kinase) fusions/rearrangements;** Given its rarity, efficacy was demonstrated by pooled analysis of three phase I/II trials involving pretreated and treatment-naïve patients with NTRK fusion-positive solid tumours for both Entrectinib (ORR 70%) (STARTRK-1 [NCT02097810], STARTRK-2 [NCT02568267] and ALKA-372-001 [EudraCT:2012-000148-88]) and Larotrectinib (ORR 75%) (NCT02122913, NCT02637687, NCT02576431).
- RET fusions/rearrangements:** Selpercatinib (RR64%; LIBRETTO-001 [NCT03157128]) and pralsetinib (ORR 61%; ARROW [NCT03037385]) are effective for RET-rearranged lung and thyroid cancers.
- ROS1 fusions/rearrangements:** Similar to the ALK timeline, Crizotinib was the first ROS1 inhibitor to be approved (phase I trial: PROFILE 1001 [NCT00585195]; ORR 72%, mPFS 19 months), with identical outcomes in another, phase II trial (NCT01945021). Unlike ALK, crizotinib effectiveness was primarily for Crizotinib-naïve patients (NCT01964157). Lorlatinib efficacy was also more pronounced for Crizotinib-naïve than Crizotinib-pretreated patients (ORR 62% versus 35%; mPFS 21 versus 8.5 months; NCT01970865). Entrectinib approval was based on pooled analysis of STARTRK-1, STARTRK-2 and ALKA-372-001 trials (ORR 67%, mPFS 16 months).

| Test Code | Test Name | Sample Requirement                            | TAT    | Method | Shipping & Stability Conditions | Clinical Utility  |
|-----------|-----------|---|--------|--------|---------------------------------|---|
| IA1337    | TTF-1     | Formalin fixed paraffin embedded tissue block | 4 Days | IHC    | Transport at ambient (18-25°C)  | Diagnosis of Thyroid/ Lung Cancer   |
| YB1290    | MET       | Formalin fixed paraffin embedded tissue block | 6 Days | FISH   | Transport at ambient (18-25°C)  | For NSCLC patients developed resistance against TKI and crizotinib therapy. |

| Test Code | Test Name              | Components                        | Sample Requirement | TAT                                | Method                | Shipping & Stability Conditions            |
|-----------|------------------------|-----------------------------------|--------------------|------------------------------------|-----------------------|--|
| P00099    | CÖREprime Lung Panel 1 | ALK (IHC) ,EGFR (PCR)             | FFPE Block         | Cut-off 1 PM, report next day 8 PM | Multiple Technologies | Transport at ambient (18-25°C) temperature |
| P00100    | CÖREprime Lung Panel 2 | EGFR (PCR), ALK (IHC), ROS1 (IHC) | FFPE Block         | Cut-off 1 PM, report next day 8 PM | Multiple Technologies | Transport at ambient (18-25°C) temperature |

| Test Code | Test Name                                   | Components             | Sample Requirement                            | TAT    | Method   | Special Instructions        | Shipping & Stability Conditions            | Clinical Utility   |
|-----------|---|------------------------|---|--------|--|-----------------------------|--|--|
| P00013    | EGFR + ALK Fusion                           | EGFR (PCR), ALK (FISH) | Formalin fixed paraffin embedded tissue block | 6 Days | Real Time Polymerase Chain Reaction & Fluorescence In Situ Hybridization | Clinical history mandatory. | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC                                       |
| ME1060    | EGFR Somatic Mutation (Exon 18-21) Analysis |                        | Formalin fixed paraffin embedded tissue block | 5 Days | Real-Time Polymerase Chain Reaction(PNA RT-PCR)                          | Clinical history mandatory. | Transport at ambient (18-25°C) temperature | For identifying non small cell lung cancer patients who could be benefited from TKI therapy. |

| Test Code | Test Name                                 | Components  | Sample Requirement | TAT     | Method   | Shipping & Stability Conditions            | Clinical Utility  |
|-----------|---|---|--------------------|---------|--|--|---|
| P00098    | Pulmo DDx Comprehensive Panel             | Pulmo DDX (IHC), EGFR Mutation Analysis (PCR), ALK (FISH)             | FFPE Block         | 6 Days  | IHC, Polymerase Chain Reaction, Fluorescence In Situ Hybridization | Transport at ambient (18-25°C)             | For diagnosis prognosis And treatment with TKI inhibitors |
| P00117    | pulmoCORE 5 Gene Panel with MET (FISH)    | EGFR, BRAF, c-MET, ALK & ROS1, MET(FISH)                              | FFPE tissue block  |         | Fluorescence In Situ Hybridization, Next Generation Sequencing     | Transport at ambient (18-25°C) temperature |   |
| NA2470    | pulmoCORE any 4 Markers (High Resolution) | Choose any 4 from the following genes (EGFR, BRAF, c-MET, ALK & ROS1) | FFPE Block         | 12 Days | Next Generation Sequencing   | Transport at ambient (18-25°C) temperature |   |
| NA2469    | pulmoCORE Basic Panel                     | EGFR, BRAF, c-MET, ALK & ROS1   | FFPE Block         | 12 Days | Next Generation Sequencing   | Transport at ambient (18-25°C) temperature |   |



| Test Code | Test Name                | Components   | Sample Requirement | TAT     | Method   | Shipping & Stability Conditions            | Clinical Utility   |
|-----------|--------------------------|--|--------------------|---------|--|--|--|
| P00141    | pulmoCORE Extended Panel | EGFR, ALK, ROS1, BRAF & MET (Next Generation Sequencing), MET (FISH), PD-L1(SP263 Ventana) IHC | FFPE Block         | 12 Days | Immunohistochemistry, Next Generation Sequencing, Fluorescence In Situ Hybridization | Transport at ambient (18-25°C) temperature | EGFR, ALK, ROS1, BRAF & MET (Next Generation Sequencing) + MET (FISH) + PDL1 IHC |
| P00020    | pulmoCORE Panel 1        | EGFR (Mutation Analysis), ALK (IHC), ROS1 (FISH)   | FFPE Block         | 6 Days  | Immunohistochemistry, Polymerase Chain Reaction, Fluorescence In Situ Hybridization  | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC                           |
| P00027    | pulmoCORE Panel 10       | EGFR, ALK (FISH), ROS-1 (FISH), MET, HER2(FISH), PDL-1 (SP263)                                 | FFPE Block         | 6 Days  | Immunohistochemistry, Polymerase Chain Reaction, Fluorescence In Situ Hybridization  | Transport at ambient (18-25°C) temperature | Diagnosis and therapy indication for lung carcinoma                              |
| P00061    | pulmoCORE Panel 11       | EGFR (Mutation analysis), ALK (IHC), ROS1 (FISH), MET (FISH)                                   | FFPE Block         | 6 Days  | Immunohistochemistry, Polymerase Chain Reaction, Fluorescence In Situ Hybridization  | Transport at ambient (18-25°C) temperature |  |
| P00187    | pulmoCORE Panel 12       | EGFR Mutation Analysis, ALK (IHC), ROS1 (FISH), PDL1 SP263 (IHC), BRAF Mutation Analysis       | FFPE Block         | 6 Days  | Immunohistochemistry, Polymerase Chain Reaction, Fluorescence In Situ Hybridization  | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC                           |
| P00019    | pulmoCORE Panel 2        | EGFR (mutation analysis), ALK (FISH), ROS-1 (FISH)   | FFPE Block         | 6 Days  | Immunohistochemistry, Polymerase Chain Reaction, Fluorescence In Situ Hybridization  | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC                           |
| P00079    | pulmoCORE Panel 4        | EGFR, ALK (FISH), ROS1 (FISH), PDL1 SP263 (IHC), BRAF  | FFPE tissue block  | 6 Days  | Immunohistochemistry, Polymerase Chain Reaction, Fluorescence In Situ Hybridization  | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC                           |

| Test Code | Test Name         | Components  | Sample Requirement                            | TAT    | Method   | Shipping & Stability Conditions            | Clinical Utility                                       |
|-----------|-------------------|---|---|--------|--|--|--|
| P00105    | pulmoCORE Panel 5 | EGFR (Mutation Analysis), ALK (FISH), ROS1 (FISH), PDL1 SP263 (IHC) | Formalin fixed paraffin embedded tissue block | 6 Days | IHC, Polymerase Chain Reaction, Fluorescence In Situ Hybridization | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC |
| P00116    | pulmoCORE Panel 6 | EGFR (Mutation Analysis), ALK (IHC), ROS1 (FISH), PDL1 SP263 (IHC)  | Formalin fixed paraffin embedded tissue block | 6 Days | IHC, Polymerase Chain Reaction, Fluorescence In Situ Hybridization | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC |
| P00026    | pulmoCORE Panel 6 | EGFR (mutation analysis), ALK (FISH), ROS1 (FISH), MET (FISH)       | Formalin fixed paraffin embedded tissue block | 6 Days | Polymerase Chain Reaction, Fluorescence In Situ Hybridization      | Transport at ambient (18-25°C) temperature | Diagnosis and therapeutic indication in cases of NSCLC |
| P00241    | pulmoCORE Panel 8 | EGFR (Mutation Analysis), ALK (IHC), ROS1 (IHC), PDL-1 22C3 (IHC)   | Formalin fixed paraffin embedded tissue block | 5 Days | IHC, Polymerase Chain Reaction                                     | Transport at ambient (18-25°C) temperature |  |

Components covered- EGFR | Mutation Analysis /ALK/ROS1 (D4D6 R) Rabbit Mab CST/PDL-1  
 For identifying non small cell lung cancer patients who could be benefited from TKI therapy.  
 Aid in identifying patients eligible for treatment with ALK Kinase Inhibitor  
 To identify NSCLC patients benefit from crizotinib therapy.

| Test Code | Test Name         | Components  | Sample Requirement                            | TAT    | Method   | Shipping & Stability Conditions            | Clinical Utility |
|-----------|-------------------|---|---|--------|--|--|------------------|
| P00242    | pulmoCORE Panel 9 | EGFR (Mutation Analysis), ALK (IHC), ROS-1 (FISH), PDL-1 22C3 (IHC) | Formalin fixed paraffin embedded tissue block | 6 Days | IHC, Polymerase Chain Reaction, Fluorescence In Situ Hybridization | Transport at ambient (18-25°C) temperature |                  |

Components covered - EGFR | Mutation Analysis /ALK/ROS1/PDL-1  
 For identifying non small cell lung cancer patients who benefited from TKI therapy.  
 Aid in identifying patients eligible for treatment with ALK Kinase Inhibitor  
 To identify NSCLC patients benefit from crizotinib therapy.

| Test Code | Test Name         | Sample Requirement                            | TAT     | Method                     |
|-----------|-------------------|---|---------|----------------------------|
| NA2726    | pulmoCORE 12 gene | Formalin fixed paraffin embedded tissue block | 10 Days | Next Generation Sequencing |

**Hotspot genes:** (SNVs and short indels): ALK, BRAF, EGFR, ERBB2, KRAS, MAP2K1, MET, NRAS, PIK3CA, RET, ROS1

and TP53.

**Gene Fusions:** ALK, METex14 skipping mutation, NTRK (1,2,3), RET and ROS1

**CNV:** MET Amplification.

| Test Code | Test Name                                     | Components                                     | Sample Requirement  | TAT     | Method   | Shipping & Stability Conditions | Clinical Utility  |
|-----------|---|--|---|---------|--|---------------------------------|---|
| P00884    | pulmoCORE 12 gene + liquiCORE lung Panel      | pulmoCORE 12 gene , liquiCORE lung Panel       | FFPE block+ 2 Streck BCT/ Paxgene Tube with 9-9.5 mL Blood each. Do not fill till the end | 15 Days | Next Generation Sequencing                       | Clinical history is mandatory   | Transport at ambient (18-25°C) temperature. For Blood: Transport at 2 to 8°C temperature. |
| P00613    | pulmoCORE 12 gene panel - 2                   | pulmoCORE 12 gene panel, PDL-1 SP263 (Ventana) | Formalin fixed paraffin embedded tissue block   | 10 Days | Next Generation Sequencing, Immunohistochemistry |                                 |   |
| P00612    | pulmoCORE 12 gene panel panel-1               | pulmoCORE 12 gene panel, PDL-1 SP142 (Ventana) | Formalin fixed paraffin embedded tissue block   | 10 Days | Next Generation Sequencing, Immunohistochemistry |                                 |   |
| P00882    | pulmoCORE 12 gene reflex liquiCORE lung Panel |  |   | 18 Days | Next Generation Sequencing                       | Clinical history is mandatory   | For Blood: Transport at 2 to 8°C temperature.   |

Formalin fixed paraffin embedded tissue block+ 2 Streck BCT/Paxgene Tube with 9-9.5 mL Blood each. Do not fill till the end so as to avoid hemolysis.

| Test Code | Test Name               | Sample Requirement                            | TAT     | Method                     |
|-----------|-------------------------|---|---------|----------------------------|
| NA2707    | pulmoCORE 20 gene Panel | Formalin fixed paraffin embedded tissue block | 15 Days | Next Generation Sequencing |

**Hotspot genes :** (SNVs and short indels): ALK, BRAF, EGFR, ERBB2, FGFR2, FGFR3, HRAS, KIT, KRAS, MAP2K1, MAP2K2, MET, MTOR, NRAS, PDGFRA, PIK3CA, RET and ROS1.

**Gene Fusions:** ALK, BRAF, EGFR, ERBB2, FGFR2, FGFR3, MET, NTRK (1,2,3), PDGFRA, RET and ROS1

**(CNV) genes:** ALK, BRAF, EGFR, ERBB2, FGFR2, FGFR3, KIT, KRAS, MET, PDGFRA, PIK3CA and MYC

# PROSTATE CARCINOMA

In metastatic prostate cancer, several mutations and therapeutic targets have been identified. Some of these include:

1. **Androgen receptor (AR) mutations:** Mutations in the AR gene can lead to resistance to hormonal therapies, such as androgen deprivation therapy (ADT). These mutations can cause the AR to be constitutively active, allowing the cancer cells to continue growing even in the absence of androgens. Therapeutic strategies targeting AR mutations include next-generation anti-androgens, such as enzalutamide and abiraterone, which can inhibit AR signaling. Fusion genes (TMPRSS2–ERG) and transcription factors (FOXP1, NKX3.1) that promote tumour-cell proliferation and survival, and prostate-specific antigen (PSA) expression.

Novel hormonal agents targeting the AR pathway, either by inhibiting steroid synthesis (abiraterone) or by AR antagonists (enzalutamide, darolutamide, apalutamide), has extended the treatment options and significantly prolonged OS in metastatic hormone-sensitive PC, and non-metastatic and metastatic castration-resistant prostate cancer (CRPC).

2. **DNA repair gene mutations:** Mutations in DNA repair genes, such as BRCA1, BRCA2, and ATM, have been found in a subset of metastatic prostate cancers. These mutations impair the ability of cells to repair DNA damage, making them more susceptible to certain targeted therapies. Poly ADP-ribose polymerase (PARP) inhibitors, such as olaparib and rucaparib, have shown efficacy in treating prostate cancers with DNA repair gene mutations.
3. **PTEN loss:** PTEN is a tumor suppressor gene that is frequently lost or mutated in prostate cancer. Loss of PTEN function can activate signaling pathways that promote cancer cell survival and growth. Therapies targeting the PI3K/AKT/mTOR pathway, such as mTOR inhibitors (e.g., everolimus) and PI3K inhibitors like buparlisib, are being investigated as potential treatments for prostate cancers with PTEN loss.

Loss of PTEN is seen in 15%–40% of PCs (depending on the detection method) and can occur as a homozygous deletion in early disease. PTEN loss is associated with aggressive metastatic disease and other adverse outcomes. A phase III trial (NCT03072238) in mCRPC patients compared ipatasertib (AKT inhibitor) plus the novel AR-targeted agent abiraterone and prednisone, versus placebo plus abiraterone and prednisone. Results reported a significantly prolonged rPFS by immunohistochemistry in the population with tumour PTEN loss.

4. **Neuroendocrine differentiation:** In some cases of metastatic prostate cancer, the cancer cells may undergo neuroendocrine differentiation, leading to a more aggressive and treatment-resistant phenotype. Therapeutic options for neuroendocrine prostate cancer include agents that target neuroendocrine markers, such as enzalutamide and platinum-based chemotherapy.
5. **Immunotherapies:** Immune checkpoint inhibitors, such as pembrolizumab and nivolumab, have shown activity in a subset of CRPC patients with mismatch repair (MMR) deficiency or high tumor mutational burden (TMB). These drugs help unleash the body's immune system to attack cancer cells.
6. **Radiopharmaceuticals:** Targeted radiopharmaceuticals, like radium-223 (Xofigo), can deliver radiation directly to bone metastases in CRPC, providing palliative benefit and potentially extending survival.

HRR (Homologous Recombination Repair) mutated cancers and BRCA (Breast Cancer) mutated cancers are related but distinct concepts. HRR mutated cancers refer to cancers that have mutations in genes involved in the homologous recombination repair pathway, which is responsible for repairing DNA double-strand breaks. These mutations can occur in various genes, such as BRCA1, BRCA2, RAD51, PALB2, and others. When these genes are mutated, the ability of cells to repair DNA damage is impaired, leading to an increased risk of developing cancer. HRR mutated cancers can occur in various types of tissues and are not limited to breast or ovarian cancers.

On the other hand, BRCA mutated cancers specifically refer to cancers that have mutations in the BRCA1 or BRCA2 genes. These genes are a subset of the HRR genes and are well-known for their association with an increased risk of breast and ovarian cancers. Mutations in BRCA1 or BRCA2 genes can significantly elevate the lifetime risk of developing these specific cancers. However, it's important to note that not all breast or ovarian cancers are caused by BRCA mutations, as other genetic and environmental factors can also contribute to the development of these cancers.

# PROSTATE

## (NEURO ENDOCRINE CARCINOMA)

Neuroendocrine carcinoma of the prostate is a rare and aggressive form of prostate cancer that is typically resistant to standard prostate cancer treatments. Due to its aggressive nature, treatment options for neuroendocrine carcinoma of the prostate may differ from those used for typical prostate adenocarcinoma.

- 1. Chemotherapy:** Chemotherapy drugs such as cisplatin and etoposide are commonly used to treat neuroendocrine carcinoma. These drugs can help shrink tumors and slow down the progression of the disease.
- 2. Hormone therapy:** Although neuroendocrine carcinoma is typically less responsive to hormone therapy compared to typical prostate adenocarcinoma, some patients may still benefit from hormone therapy drugs such as androgen receptor antagonists or LHRH agonists.
- 3. Targeted therapy:** Targeted therapies that specifically target certain genetic mutations or proteins may be considered. For example, PARP inhibitors or immunotherapy drugs may be used in some cases.
- 4. Radiation therapy:** Radiation therapy may be used to help relieve symptoms or target specific areas where the cancer has spread, such as bone metastases.

Table 3: Comparison of gene testing strategies [9, 43]

| Method of Testing | Sample Required                 | Advantage  | Limitations  |
|-------------------|---------------------------------|--|--|
| Germline Testing  | Blood or Saliva                 | <ul style="list-style-type: none"> <li>Germline mutations detected reliably</li> <li>Large panels of tests available which can detect germline mutations in mCRPC</li> </ul>   | Unable to detect somatic mutations relevant to treatment selection   |
| Somatic Testing   | Tumor Tissue/ metastatic tissue | <ul style="list-style-type: none"> <li>Can detect germline and somatic mutations,</li> <li>Tumor heterogeneity might result which might be relevant for initiating targeted therapies</li> <li>Provides information about translocations and amplifications</li> <li>A multigene panel of tests available with testing for &gt;300 genes possible</li> </ul> | Tumor heterogeneity might result in missing late somatic mutations especially if testing is conducted on archival sample. Somatic testing is less sensitive, and thus robustly validated somatic testing is require  |
| Ct DNA Testing    | Plasma                          | <ul style="list-style-type: none"> <li>Can identify germline and somatic mutations relevant for targeted therapies.</li> <li>Minimally invasive process for sample in collection as the biomaterial required is blood</li> <li>Provides insight into the subclonal population</li> <li>Gene that may be more relevant to current disease</li> </ul>          | <ul style="list-style-type: none"> <li>Not enough evidence about shedding in mCRPC pattern of cDNA in blood circulation</li> <li>Availability of robustly validated HRR gene panetest</li> <li>Panels may not have nonactionable genes still relevantor PCa</li> <li>Chance of missing a germline variant if not sequencing the whole gene due to small size of ctDNA</li> </ul> |

| Test Code | Test Name              | TAT    | Method | Special Instructions   | Shipping & Stability Conditions            |
|-----------|------------------------|--------|--------|--|--|
| IA1193    | Androgen Receptor (AR) | 4 Days | IHC    | Clinical history, Histopathology report, Any radiological findings | Transport at ambient (18-25°C) temperature |

| Test Code | Test Name | Sample Requirement                            | TAT    | Shipping & Stability Conditions            | Clinical Utility                       |
|-----------|-----------|---|--------|--|--|
| IA1860    | ERG       | Formalin fixed paraffin embedded tissue block | 4 Days | Transport at ambient (18-25°C) temperature | Diagnosis of Prostatic Adeno Carcinoma |

| Test Code | Test Name                     | Sample Requirement  | TAT    | Special Instructions                       |
|-----------|-------------------------------|---|--------|--|
| YB2535    | NTRK 1/2/3 Fusions Gene Panel | Submit formalin fixed paraffin embedded tissue block or three 4 micron sections on Poly-L-Lysine coated slides. | 5 Days | Transport at ambient (18-25°C) temperature |

| Test Code | Test Name | Sample Requirement                            | TAT    | Method | Shipping & Stability Conditions            |
|-----------|-----------|---|--------|--------|--|
| IA1425    | AMACR     | Formalin fixed paraffin embedded tissue block | 4 Days | IHC    | Transport at ambient (18-25°C) temperature |

| Test Code | Test Name                           | Sample Requirement | TAT  | Method    | Shipping & Stability Conditions   |
|-----------|-------------------------------------|--------------------|--|-----------|---|
| OA2670    | Homologous Recombination Deficiency | HOXB               | FFPE+ 4ml Peripheral Blood (EDTA vacutainer) | 3-4 Weeks | MLPA, Next Generation Sequencing<br>Ambient (18-25°C) temperature. Do not Freeze. |

| Test Code | Test Name                                     | Sample Requirement  | TAT     | Special Instructions | Shipping & Stability Conditions            |
|-----------|---|---|---------|----------------------|--|
| NA2452    | BRCA1 and BRCA2 Somatic Gene Sequencing Panel | Formalin fixed paraffin embedded tissue block or at least 10 section of accompanying pathology report | 15 Days | NGS                  | Transport at ambient (18-25°C) temperature |

| Test Code | Test Name                          | Sample Requirement                     | TAT     | Method                     | Special Instructions          | Shipping & Stability Conditions        |
|-----------|------------------------------------|--|---------|----------------------------|-------------------------------|--|
| NA3166    | HRR Gene Panel (Germline) Extended | 2ml Peripheral Blood (EDTA Vacutainer) | 2 Weeks | Next Generation Sequencing | Clinical history is mandatory | Transport in 2 to 8°C (with cold pack) |

ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCD2, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD54L, TP53, CHEK1, FANCL, RAD50, RAD51, RAD51C, RAD51D, RAD52, XRCC2, KRAS, PIK3CA, POLD1, POLE, PTEN

| Test Code | Test Name                          | Sample Requirement            | TAT     | Method | Special Instructions           | Shipping & Stability Conditions                     |
|-----------|------------------------------------|-------------------------------|---------|--------|--------------------------------|---|
| NA3163    | HRR Somatic reflex to HRR Germline | FFPE block + Peripheral Blood | 16 Days | NGS    | Clinical history is mandatory. | Tissue-Ambient (18-25°C) temperature. Do not Freeze |

ATM, MRE11, BARD1, NBN, BRCA1, PALB2, BRCA2, PPP2R2A, BRIP1, RAD51B, CDK12, RAD54L, CHEK2, TP53, FANCD2, RAD51C, RAD51D

| Test Code | Test Name                         | Sample Requirement | TAT     | Method | Special Instructions           | Shipping & Stability Conditions              |
|-----------|-----------------------------------|--------------------|---------|--------|--------------------------------|--|
| NA3167    | HRR Gene Panel (Somatic) Extended | FFP                | 2 Weeks | NGS    | Clinical history is mandatory. | Ambient (18-25°C) temperature. Do not Freeze |

ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCD2, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD54L, TP53, CHEK1, FANCL, RAD50, RAD51, RAD51C, RAD51D, RAD52, XRCC2, KRAS, PIK3CA, POLD1, POLE, PTEN

| Test Code | Test Name                | Sample Requirement | TAT     | Method | Special Instructions                         |
|-----------|--------------------------|--------------------|---------|--------|--|
| NA2577    | HRR Gene Panel (Somatic) | FFPE               | 2 weeks | NGS    | Ambient (18-25°C) temperature. Do not Freeze |

ATM, MRE11, BARD1, NBN, BRCA1, PALB2, BRCA2, PPP2R2A, BRIP1, RAD51B, CDK12, RAD54L, CHEK2, TP53, FANCD2, RAD51C, RAD51D

| Test Code | Test Name                          | Sample Requirement                     | TAT     | Method | Special Instructions           | Shipping & Stability Conditions        |
|-----------|------------------------------------|--|---------|--------|--------------------------------|--|
| NA3166    | HRR Gene Panel (Germline) Extended | 2ml Peripheral Blood (EDTA Vacutainer) | 2 Weeks | NGS    | Clinical history is mandatory. | Transport in 2 to 8°C (with cold pack) |

ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCD2, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD54L, TP53, CHEK1, FANCL, RAD50, RAD51, RAD51C, RAD51D, RAD52, XRCC2, KRAS, PIK3CA, POLD1, POLE, PTEN

| Test Code | Test Name                 | Sample Requirement                     | TAT     | Method | Special Instructions           | Shipping & Stability Conditions               |
|-----------|---------------------------|--|---------|--------|--------------------------------|---|
| NA2579    | HRR Gene Panel (Germline) | 2ml Peripheral Blood (EDTA Vacutainer) | 2 Weeks | NGS    | Clinical history is mandatory. | Ambient (18-25°C) temperature. Do not Freeze. |

ATM, MRE11, BARD1, NBN, BRCA1, PALB2, BRCA2, PPP2R2A, BRIP1, RAD51B, CDK12, RAD54L, CHEK2, TP53, FANCD2, RAD51C, RAD51D

| Test Code | Test Name | Sample Requirement     | TAT     | Method | Special Instructions           | Shipping & Stability Conditions               |
|-----------|-----------|------------------------|---------|--------|--------------------------------|---|
| P00397    | FUS-DDIT3 | FFPE+ Peripheral Blood | 2 Weeks | NGS    | Clinical history is mandatory. | Ambient (18-25°C) temperature. Do not Freeze. |

ATM, MRE11, BARD1, NBN, BRCA1, PALB2, BRCA2, PPP2R2A, BRIP1, RAD51B, CDK12, RAD54L, CHEK2, TP53, FANCD2, RAD51C, RAD51D

| Test Code | Test Name                                    | Sample Requirement            | TAT     | Method | Special Instructions           | Shipping & Stability Conditions  |
|-----------|--|-------------------------------|---------|--------|--------------------------------|--|
| P01065    | HRR Gene Panel (Somatic + Germline) Extended | FFPE block + Peripheral Blood | 2 Weeks | NGS    | Clinical history is mandatory. | Tissue-Ambient (18-25°C) temperature. Do not Freeze. +Blood-Transport in 2 to 8°C (with cold pack) |

ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCD2, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD54L, TP53, CHEK1, FANCL, RAD50, RAD51, RAD51C, RAD51D, RAD52, XRCC2, KRAS, PIK3CA, POLD1, POLE, PTEN

# RENAL CELL CA

Clear Cell RCC – Multiples Kinases Involved in the Angiogenesis Pathway.

**VEGF:** VEGF-C and its receptor, VEGFR-3, are involved in lymph- angiogenesis. Expression of these receptors is seen in endothelial and tumour cells. VEGF-C can induce lymphangiogenesis, lymphovascular invasion and metastasis.

**PDGF** (Platelet-derived growth factor): promotes tumour neoangiogenesis, which plays a role in tumour progression. PDGF is induced by inactivation of the VHL pathway. High expression of PDGF-β in tumour tissue is associated with poor prognosis for patients with clear cell RCC (ccRCC).

**FGFs** (Fibroblast growth factor): FGFs and FGFR2 regulate cellular proliferation, survival, migration and differentiation, but also promote the formation of blood vessels and are upregulated upon resistance to VEGF-targeted treatment. Endothelial cells respond to FGFs via integrins (cell adhesion) and promote cell adhesion and proliferation. FGF/FGFR signalling plays a role in angiogenesis, mitosis and proliferation in the RCC pathway.

**mTOR** (Mammalian target of Rapamycin): PI3K/AKT/mTOR pathway activation is a result of signal transduction by growth factors. Genitourinary Malignancies 159

It is one of the signalling pathways characteristic of most cells. Phosphatase and tensin homologue (PTEN) is a key suppressor of the PI3K/AKT/mTOR signalling cascade. Its mutations and deletion in primary RCC have been associated with an increased risk of metastasis.

**HIF 2 alpha (HIF-2α):** The VHL protein (pVHL) is closely related to ccRCC carcinogenesis, as is its function as a subunit of the E3 ubiquitin ligase complex, which mediates the degradation of HIF-2α. Under hypoxic conditions, HIF-2α forms an active transcription factor (by binding to HIF-1β) that upregulates expression of hypoxia-inducible genes, such as VEGF.

| Test Code  | Test Name              | Sample Requirement                            | TAT     | Method | Special Instructions  | Shipping & Stability Conditions            | Clinical Utility                  |
|--|------------------------|---|---------|--------|---|--|-----------------------------------|
| IA1787   | PAX2                   | Formalin fixed paraffin embedded tissue block | 4 Days  | IHC    | Clinical History, Histopathology Report, Any Radiological Findings required | Transport at ambient (18-25°C) temperature | Diagnosis of Renal Cell Carcinoma |
| MM1788   | Wilms tumor (WT1) gene | EDTA Whole Blood / EDTA Bone Marrow 3ml       | 10 Days | IHC    | Clinical history is mandatory   | Transport in 2 to 8°C (with cold pack)     |                                   |
| IA1788   | WT1 (Wilms Tumor)      | Formalin fixed paraffin embedded tissue block | 4 Days  | IHC    | Clinical History, Histopathology Report, Any Radiological Findings required | Transport at ambient (18-25°C) temperature | Diagnosis of Kidney Tumors        |
| <p>Wilm's tumour suppressor gene1 (WT1) causes an embryonic malignancy of the kidney. It occur in both sporadic and hereditary forms. Inactivation of WT1 causes Wilm's tumour, and Denys-Drash syndrome (DDS), leading to nephropathy and genital abnormalities</p> |                        |   |         |        |   |  |                                   |



# PAILLARY UROTHELIAL CARCINOMA

## (PRCC Type 1 and Type 2)

| Test Code | Test Name | Sample Requirement                            | TAT    | Method | Special Instructions                       | Shipping & Stability Conditions  |
|-----------|-----------|---|--------|--------|--|--|
| IA1437    | CK7       | Formalin fixed paraffin embedded tissue block | 4 Days | IHC    | Transport at ambient (18-25°C) temperature | Diagnosis of Lung, Salivary gland, Uterus, Thyroid, Breast, Ovary<br>Type 1 Papillary Renal Cell CA (pRCC) |

| Test Code | Test Name  | Sample Requirement                            | TAT    | Method | Special Instructions  | Shipping & Stability Conditions  | Clinical Utility  |
|-----------|------------|---|--------|--------|---|--|---|
| IA1435    | CK20       | Formalin fixed paraffin embedded tissue block | 4 Days | IHC    | Clinical History, Histopathology Report, Any Radiological Findings required | Transport at ambient (18-25°C) temperature   | Diagnosis of Large Intestinal Cancers.,                           |
| IA1440    | E-Cadherin | FFPE block                                    | 4 Days | IHC    | Clinical History, Histopathology Report, Any Radiological Findings required | Transport at ambient (18-25°C) temperature   | Diagnosis of Breast cancer, Type 2 Papillary Renal Cell CA (pRCC) |
| IA1425    | AMACR      | FFPE block                                    | 4 Days | IHC    | Transport at ambient (18-25°C) temperature                                  | AMACR (P504S) is a positive marker for Prostatic adenocarcinomas which along with basal cell markers like 34 Beta E12 and p63 helps to confirm the diagnosis of a small focus of prostate carcinoma in needle biopsies. Expressed in Papillary Renal Cell Carcinoma. |   |

<https://www.sciencedirect.com/topics/medicine-and-dentistry/papillary-renal-cell-carcinomas>

# EPITHELIAL UROTHELIAL CARCINOMA

CDKN2A is a tumor suppressor gene. It is a Variants of Uncertain Significance (VUS) here. CTNNB1 explains the possibility of this cancer being hereditary. It's a rare mutation, but if found they are extremely sensitive to Cisplatin, Cyclophosphamide, Vincristine, Gemcitabine, and Radiation Therapy. ( Here it is detected and pathogenic) Since PIK3CA [NM\_006218.4] is detected and pathogenic, it would respond to ALPELISIB in advanced or metastatic stage.

| Gene (Exon) [Transcript]    | Variant (Amino acid Alteration) | Variant (Coding) | Variant Allele Frequency (VAF) | Variant Effect* | Variant Classification (AMP) | Variant Classification (ACMG)# | Associated FDA Approved Therapies                       |
|-----------------------------|---------------------------------|------------------|--------------------------------|-----------------|------------------------------|--------------------------------|---|
| PIK3CA (10) [NM_006218.4]   | p.Glu545Lys (p.E545K)           | c.1633G>A        | 10.9%                          | GOF             | Tier2                        | Pathogenic                     | Available (Please refer to page no. 2 for more details) |
| CTNNB1 (3) [NM_001904.4]    | p.Ser45Phe [p.S45F]             | c.134C>T         | 8.2%                           | GOF             | Tier2                        | Pathogenic                     | NA  |
| TP53 (5) [NM_000546.6]      | p.Cys135Tyr (p.C135Y)           | c.404G>A         | 8.9%                           | LOF             | Tier1                        | Likely pathogenic              | NA  |
| CDKN2A (2) [NM_001195132.2] | p.His83Tyr (p.H83Y)             | c.247C>T         | 12.1%                          | —               | Tier3                        | VUS                            | NA  |

| Trial  | Experimental Therapy                                  | Control Arm | Primary End Point                               | Pfs   | Os   |
|--|---|-------------|---|---|--|
| Sunitinib vs IFN- $\alpha$<br>n=750<br>NCT00083889 | Sunitinib   | Everolimus  | PFS   | 11 vs 5 mo<br>CHR 0.42, 95% CI 0.32-0.54, p < 0.001)        | 26.4 vs 21.8 mo CHR<br>0.821, 95% CI<br>0.673-1.001, p = 0.05)   |
| Sunitinib vs pazopanib<br>n=1110<br>NCT00720941    | Pazopanib   | Sunitinib   | PFS (non-inferiority)                           | 8.4 vs 9.5 mo<br>CHR 1.05, 95% CI 0.90-1.22)                | 28.4 vs 29.3 mo<br>CHR 0.91, 95% CI 0.76-1.08, p = 0.28)         |
| Tivozanib vs sorafenib<br>n=517<br>NCT01030783     | Tivozanib   | Sorafenib   | PFS   | 11.9 vs 9.1 mo<br>(HR 0.797, 95% CI 0.639-0.993, p = 0.042) | 28.8 vs 29.3 mo<br>(HR 1.245, 95% CI 0.954-1.624, p = 0.105)     |
| CheckMate 214<br>n=1096<br>NCT02231749             | Ipilimumab + nivolumab                                | Sunitinib   | PFS, OS IMDC risk score: intermediate/poor RISK | 11.6 vs 8.3 mo<br>(HR 0.75, 95% CI 0.62-0.90, p = 0.0015)   | 55.7 vs 38.4 mo<br>(HR 0.72, 95% CI 0.62-0.85, p < 0.0001)       |
| KEYNOTE-426<br>n=961<br>NCT02853331                | Pembrolizumab + axitinib                              | Sunitinib   | PFS /OS   | 15.7 vs 11.1 mo<br>(HR 0.68, 95% CI 0.58-0.8, p < 0.0001)   | 45.7 vs 40.1 mo<br>(HR 0.73, 95% CI 0.60-0.88), p < 0.001)       |
| CheckMate 9ER<br>n=651<br>NCT03141177              | Nivolumab + cabozantinib                              | Sunitinib   | PFS   | 16.6 vs 8.3 mo<br>(HR 0.51, 95% CI 0.41-0.64, p < 0.001)    | 37.7 vs 34.3 mo<br>CHR 0.7, 95% CI 0.55-0.9, p = 0.001)          |
| CLEAR<br>n=1069<br>NCT04704219                     | Pembrolizumab + lenvatinib vs Lenvatinib + Everolimus | Sunitinib   | PFS   | 23.9 vs 9.2 mo<br>(HR 0.39, 95% CI 0.32-0.49, p < 0.001)    | 24 mo: 79.2% vs 70.496<br>(HR 0.66, 95% CI 0.49-0.88, p = 0.005) |

# THYROID CA

| Test Code | Test Name | Sample Requirement                            | TAT    | Method | Special Instructions  | Shipping & Stability Conditions            | Clinical Utility                 |
|-----------|-----------|---|--------|--------|---|--|----------------------------------|
| IA1337    | TTF-1     | Formalin fixed paraffin embedded tissue block | 4 Days | IHC    | Clinical History, Histopathology Report, Any Radiological Findings required | Transport at ambient (18-25°C) temperature | Diagnosis of Thyroid/Lung Cancer |

| Test Code | Test Name                 | Sample Requirement                            | TAT    | Method                             | Special Instructions          | Shipping & Stability Conditions            |
|-----------|---------------------------|---|--------|------------------------------------|-------------------------------|--|
| YB2534    | NTRK 1 Gene Rearrangement | Formalin fixed paraffin embedded tissue block | 5 Days | Fluorescence In Situ Hybridization | Clinical history is mandatory | Transport at ambient (18-25°C) temperature |

NTRK1 rearrangements have been shown to be involved in thyroid carcinogenesis. Several studies show that NTRK1 rearrangements may be associated with a worse clinical course when compared with NTRK1 rearrangement-negative Papillary Thyroid Carcinomas. The treatment of patients with NTRK fusion-positive cancers with a NTRK inhibitor, such as the FDA approved drugs Larotrectinib or Entrectinib, is associated with high response rates regardless of NTRK gene, fusion partner, and tumor type. Hence, detection of NTRK1 rearrangements by in situ Hybridization may be of prognostic and therapeutic significance.

# PANCREAS CA

Several genes are targeted in pancreatic cancer treatment, including:

- KRAS:** Mutations in the KRAS gene are found in the majority of pancreatic cancers, making it a prime target for therapeutic interventions aimed at inhibiting the aberrant signaling pathways associated with KRAS mutations.
- EGFR (Epidermal Growth Factor Receptor):** Drugs like erlotinib target EGFR, which is overexpressed in some pancreatic cancers. These drugs work by blocking the signaling pathways that promote cancer cell growth and proliferation.
- BRCA1/BRCA2:** PARP inhibitors, such as olaparib, are used in patients with pancreatic cancer who have mutations in the BRCA1 or BRCA2 genes. These drugs exploit deficiencies in DNA repair mechanisms to selectively kill cancer cells.
- mTOR (Mammalian Target of Rapamycin):** Everolimus is an mTOR inhibitor that can be used in pancreatic cancer treatment to block the mTOR signaling pathway, which is involved in cell growth and survival.
- HER2 (Human Epidermal Growth Factor Receptor 2):** Some pancreatic cancers overexpress HER2, making them potential targets for HER2-targeted therapies such as trastuzumab.

These are just a few examples, and ongoing research continues to identify new targets for pancreatic cancer treatment.

| Test Code | Test Name                     | Components                                      | Sample Requirement  | TAT    | Method | Shipping & Stability Conditions            |
|-----------|-------------------------------|---|---|--------|--------|--|
| YB2535    | NTRK 1/2/3 Fusions Gene Panel | NTRK1 (1q21.3), NTRK2 (9q21.3), NTRK3 (15q25.3) | Submit formalin fixed paraffin embedded tissue block or three 4 micron sections on Poly-L-Lysine coated slides. | 5 Days | FISH   | Transport at ambient (18-25°C) temperature |

| Test Code | Components  | Sample Requirement   | TAT     | Method                          |
|-----------|---|--|---------|---------------------------------|
| P00616    | TP53, KRAS, NRAS, BRAF, ERBB2, NTRK(1,2,3), PIK3CA, MSI-PCR | Formalin-fixed paraffin-embedded tissue block, 3 mL Peripheral Blood in EDTA (Lavender Top) Tube | 15 Days | Next Generation Sequencing, PCR |

Gene rearrangements that involve NTRK1/2/3 can generate fusion oncoproteins that contain the kinase domains of TRKA/B/C, respectively. In NSCLC, NTRK fusions are estimated to occur at a frequency of approximately 0.1% to 1%. The TRK inhibitors namely, Larotrectinib (LOXO-101) and Entrectinib (RXDX-101) are oral tyrosine kinase inhibitor that have high selectivity and potency for TRKA, TRKB, and TRKC. The detection of NTRK1/2/3 translocations by Fluorescence in situ Hybridization (FISH) may be of diagnostic and therapeutic relevance.

| Test Code | Test Name          | Components         | Sample Requirement | TAT    | Method | Special Instructions   | Shipping & Stability Conditions            |
|-----------|--------------------|--------------------|--------------------|--------|--------|--|--|
| P00078    | ALK IHC + ROS1 IHC | ALK IHC + ROS1 IHC | FFPE               | 4 Days | IHC    | Clinical history, Histopathology report, any radiological findings | Transport at ambient (18-25°C) temperature |

| Test Code | Components                                    | Sample Requirement   | TAT     | Method                     | Shipping & Stability Conditions            |
|-----------|---|--|---------|----------------------------|--|
| NA2452    | BRCA1 and BRCA2 Somatic Gene Sequencing Panel | Formalin fixed paraffin embedded tissue block or at least 10 section of Formalin fixed paraffin embedded tissue block of thickness 5-10µm with marked area of enriched tumor and accompanying pathology report | 15 Days | Next Generation Sequencing | Transport at ambient (18-25°C) temperature |

| Test Code | Test Name | Sample Requirement  | TAT    | Method | Special Instructions                   | Shipping & Stability Conditions  | Clinical Utility   |
|-----------|-----------|---|--------|--------|--|--|--|
| MM1119    | MSI       | Formalin fixed paraffin embedded tissue block, 3 mL Peripheral Blood in EDTA (Lavender Top) Tube. | 6 Days | PCR    | Clinical history, Medical prescription | Blood : Stable at - 4°C for 72 hrs, FFPE Block : Ambient temperature. Transport in 2 to 8°C (with cold pack). Stable at 4°C for 1 week | Microsatellite instability (MSI) is a hypermutable 15% of all colorectal cancers; 3% are of these are associated with Lynch syndrome and the other 12% are caused by sporadic, acquired hypermethylation of the promoter of the MLH1 gene, which occurs in tumors with the CpG island methylator phenotype |

Some current drugs used in the treatment of pancreatic cancer include:

- Gemcitabine:** A chemotherapy drug often used as a first-line treatment for pancreatic cancer.
- Abraxane (nab-paclitaxel):** Another chemotherapy drug commonly used in combination with gemcitabine for the treatment of pancreatic cancer.
- FOLFIRINOX:** A chemotherapy regimen consisting of a combination of drugs including folinic acid, fluorouracil, irinotecan, and oxaliplatin. It is used for advanced pancreatic cancer.
- Erlotinib:** A targeted therapy drug that inhibits the epidermal growth factor receptor (EGFR), used in combination with gemcitabine for advanced pancreatic cancer.
- Everolimus:** An mTOR inhibitor used in cases where standard chemotherapy has failed.
- Olaparib:** A PARP inhibitor used in pancreatic cancer patients with BRCA mutations.
- Trastuzumab:** A targeted therapy drug used in pancreatic cancer patients whose tumors overexpress the HER2/neu protein.

These drugs are often used in combination with each other or with other treatment modalities such as surgery and radiation therapy, depending on the stage and characteristics of the cancer. Treatment decisions are made on a case-by-case basis by healthcare providers. Some current drugs used in the treatment of pancreatic cancer include:

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# CNS /GLIOMAS

Some targeted therapy options are available for patients with selected CNS tumours. Oncogenic NTRK fusions are primarily described in paediatric gliomas of all grades, ependymoma, glioneuronal tumours and adult glioblastoma.

Although only a small subpopulation of tumours harbour NTRK fusions, they represent a viable target for personalised treatment approaches. Intracranial activity of NTRK inhibitors was shown in paediatric and adult primary brain tumours with an acceptable safety profile

| Test Code | Test Name                   | Sample Requirement | TAT     | Method                             | Special Instructions   | Shipping & Stability Conditions            | Clinical Utility   |
|-----------|-----------------------------|--------------------|---------|------------------------------------|--|--|--|
| ME1102    | MGMT                        | FFPE tissue block  | 10 Days | Methylation Specific PCR           | Clinical History is mandatory.                                     | Transport at ambient (18-25°C) temperature | It is a strong predictive factor of favourable survival in Glioblastoma multiforme (GBM) patients undergoing chemotherapy with alkylating agents.  |
| YB1104    | 1p/19q (co-deletion)        | FFPE tissue block  | 7 Days  | Fluorescence In Situ Hybridization | Clinical history is mandatory                                      | Transport at ambient (18-25°C) temperature | Oligodendroglioma tumors exhibit simultaneous deletions of 1p and 19q in two thirds of cases. These deletions have been associated with a favorable response to chemotherapy with long survival.   |
| IA1395    | ATRX                        | FFPE tissue block  | 4 Days  | IHC                                | Clinical history, Histopathology report, Any radiological findings | Transport at ambient (18-25°C) temperature | Astrocytomas - diagnostic, predictive, and prognostic marker applications  |
| MM1101    | IDH 1 & 2 Mutation Analysis | FFPE               | 8 Days  | PCR Sequencing                     |  | Transport at ambient (18-25°C)             | The IDH1 mutations are considered to be the earliest events in the development of oligodendrogliomas. IDH-mutated cancers are associated with younger age at diagnosis in most glioma tumor. Glioma patients with IDH mutations survive longer than patients with wild-type IDH. |
| IA1103    | IDH 1 R132H                 | FFPE Block         | 4 Days  | IHC                                | History, Histopathology report. Any radiological findings          | Transport at ambient (18-25°C) temperature | Distinguish reactive Gliosis from Low Grade Glioma   |

Table 1. Overview on NTRK Inhibitor Trials in Glioma.

| Disease Entity   | Drug          | Response Rate         | Survival/DoR                            | NCT Trial Number           |
|--|---------------|-----------------------|---|----------------------------|
| Glioma, glioblastoma, astrocytoma, not otherwise specified   | Larotrectinib | ORR: 11%<br>DCR: 100% | DoR: 2.8-9.2 mo                         | NCT02637687<br>NCT02576431 |
| High-grade glioma, low-grade glioma, glioneuronal tumours, neuroepithelial tumours, CNS neuroblastoma, small round blue cell tumours | Larotrectinib | ORR: 30%<br>DCR: 73%  | Median PFS: 18.3 mo<br>DoR: not reached | NCT02637687<br>NCT02576431 |
| CNS tumours (paediatric), not otherwise specified  | Entrectinib   | ORR: 75%              | Not reported                            | NCT02650401                |

Abbreviations: CNS, central nervous system; DCR, disease control rate; DoR, duration of response; mo, months; NTRK, neurotrophic tyrosine receptor kinase; ORR, overall response rate; PFS, progression-free survival.

Table 2. Overview of Trials in BRAF-mutant Brain Tumours.

| Disease Entity   | Drug                                      | Response Rate                                       | Survival/DoR   | NCT Trial Number           |
|--|---|---|--|----------------------------|
| BRAF V600E-mutant gliomas (diffuse glioma, glioblastoma, pleomorphic xanthoastrocytoma, anaplastic ganglioglioma, pilocytic astrocytoma, not otherwise specified, high-grade glioma) | Vemurafenib                               | ORR: 25%  | Median PFS: 5.5 mo                                     | NCT02637687<br>NCT02576431 |
| BRAF V600E-mutant paediatric low-grade glioma  | Dabrafenib                                | ORR: 41%  | Not reported   | NCT02637687<br>NCT02576431 |
| BRAF V600E-mutant high-grade glioma  | Dabrafenib + trametinib (MEK inhibitor)   | ORR: 26%  | Median PFS: 1.9 mo<br>DoR: 212 mo in 62.5% of patients | NCT02650401                |
| Papillary craniopharyngioma (BRAF-mutant)  | Vemurafenib + cobimetinib (MEK inhibitor) | ORR: 93% (central review),<br>93.75% (local review) | Median PFS: not reached                                | NCT03224767                |

Abbreviations: CNS, central nervous system; DCR, disease control rate; DoR, duration of response; mo, months; NTRK, neurotrophic tyrosine receptor kinase; ORR, overall response rate; PFS, progression-free survival.

Table 3. Overview of Trials in IDH-mutant Gliomas.

| Disease Entity             | Drug       | Response Rate   | Survival/DoR  | NCT Trial Number |
|----------------------------|------------|---|---|------------------|
| Diffuse glioma, IDH-mutant | Ivosidenib | Non-contrast enhancing glioma:<br>ORR: 2.9%<br>DCR: 85.7%<br>Contrast enhancing glioma:<br>DCR: 45.2% | Non-contrast enhancing glioma:<br>Median PFS: 13.6 mo<br>Contrast enhancing glioma:<br>Median PFS: 1.4 mo | NCT02073994      |

| Disease Entity                           | Drug        | Response Rate                     | Survival/DoR  | NCT Trial Number |
|--|-------------|-----------------------------------|---|------------------|
| Diffuse glioma, IDH-mutant               | Vorasidenib | ORR: 13.6%<br>SD: 77.3%           | 60.5% of patients were progression-free and alive at 24 months. | NCT02481154      |
| Astrocytoma, WHO grade 3 or4, IDH-mutant | IDH1-vac    | Peripheral immune response: 93.3% | 63% 3-year PFS  | NCT02454634      |

Abbreviations: DCR, disease control rate; DoR, duration of response; IDH, isocitrate dehydrogenase; IDH1-vac, IDH1 (R132H) peptide vaccine; mo, months; ORR, overall response rate; PFS, progression-free survival; SD, stable disease; WHO, World Health



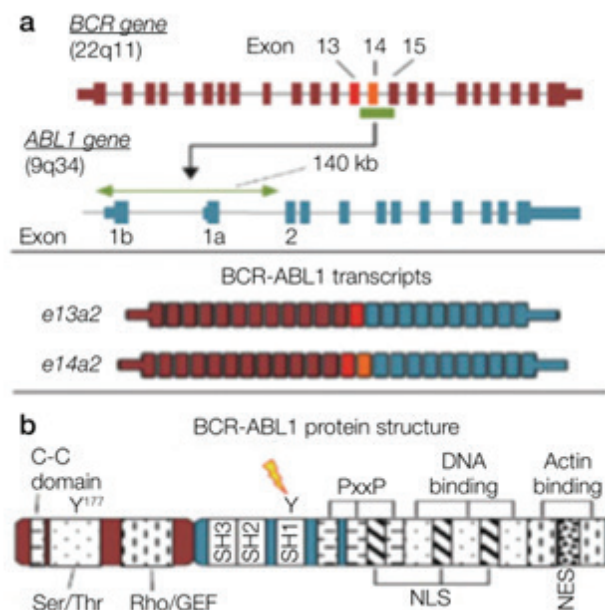
## SMALL ROUND CELL TUMORS

| Test Code | Test Name                             |          | Sample Requirement                            | TAT    | Method | Special Instructions  | Shipping & Stability Conditions            | Clinical Utility   |
|-----------|---------------------------------------|----------|---|--------|--------|---|--|--|
| IA1791    | Beta-catenin (EP35 Rabbit Monoclonal) | \$ 32.26 | Formalin fixed paraffin embedded tissue block | 4 Days | IHC    | Clinical History, Histopathology Report, Any Radiological Findings required | Transport at Ambient (18-25°C) temperature | Overexpression of beta-catenin, a cytoplasmic signaling protein, is characteristic of neuroblastoma, in contrast to most other small round blue cell tumors. Desmoid tumors may show both nuclear and cytoplasmic expression for beta-catenin. |

## MESOTHELIOMA

| Test Code | Test Name        |          | Sample Requirement                            | TAT    | Method | Special Instructions  | Shipping & Stability Conditions            | Clinical Utility   |
|-----------|------------------|----------|---|--------|--------|---|--|--|
| IA1796    | Ber- Ep4 (EpCAM) | \$ 32.26 | Formalin fixed paraffin embedded tissue block | 4 Days | IHC    | Clinical History, Histopathology Report, Any Radiological Findings required | Transport at Ambient (18-25°C) temperature | Differential diagnosis of mesothelioma versus adenocarcinoma |

## CHRONIC MYELOID LEUKAEMIA



The prevalence of CML will almost double in the next 30 years, due to survival improvement and increasing life expectancy.

Three bcr/abl1 TKIs are registered and available in most European countries as first-line therapy for CML in ie: Imatinib, Nilotinib , Dasatinib. The second-generation TKIs Nilotinib and Dasatinib reveal faster cytogenetic and molecular responses compared with imatinib; the 5-year overall survival is, however, not statistically significantly DIFFERENT.

| Test Code | Test Name   | Components  | Sample Requirement   | TAT     | Method                     | Shipping & Stability Conditions        |
|-----------|---|---|--|---------|----------------------------|--|
| NA2873    | Chronic Myeloproliferative Disorder Gene Panel (CMPD) | Hotspot genes: ABL1, CBL, CSF3R, JAK2, KIT, MPL<br>Full genes: CALR<br>Gene fusions: PDGFRA | 5 mL Bone marrow/ Peripheral Blood in EDTA(Lavender Top) in two separate vials | 15 Days | Next Generation Sequencing | Transport in 2 to 8°C (with cold pack) |

We can find BCR-ABL1 for CML; JAK2V617F & JAK2 exon 12 in V617F-negative case for Polycythemia Vera; JAK2V617F, CALR, MPLW515 for Primary myelofibrosis (PMF) & Essential thrombocythemia (ET); PDGFRA Fusion for CEL/HES, CSF3R for Chronic neutrophilic leukemia.

| Test Code | Test Name                              | Sample Requirement   | TAT    | Special Instructions           | Shipping & Stability Conditions                       | Clinical Utility   |
|-----------|--|--|--------|--------------------------------|---|--|
| YB1122    | PDGFRA, (4q12) Gene Rearrangement      | 3-4 ml Bone Marrow/ Peripheral Blood in EDTA(Lavender Top), Sodium heparin (Green Top) Tube. | 7 Days | Clinical history is mandatory. | Transport in 2 to 8°C (with cold pack) within 72 hrs. | For diagnosis of myeloproliferative/ myelodysplastic syndrome with eosinophilia. |
| YB1121    | PDGFRB, (5q32-5q33) Gene Rearrangement | 3-4 ml Bone Marrow/ Peripheral Blood in EDTA(Lavender Top), Sodium heparin (Green Top) Tube. | 7 Days | Clinical history is mandatory. | Transport in 2 to 8°C (with cold pack) within 72 hrs. | For diagnosis of myeloproliferative/ myelodysplastic syndrome with eosinophilia. |

| Test Code | Test Name                       | Sample Requirement   | TAT     | Method                                | Special Instructions   | Shipping & Stability Conditions                                     | Clinical Utility  |
|-----------|---------------------------------|--|---------|---------------------------------------|--|---|---|
| MM1003    | BCR-ABL Kinase Domain Mutations | 3-4 mL Bone marrow/ Peripheral Blood in EDTA (Lavender Top) Tube | 7 Days  | Polymerase Chain Reaction, Sequencing | Clinical history is mandatory, Old report number (if done from same lab) | Stable at 4°C for 72 hours. Transport in 2 to 8°C (with cold pack). | Detection of mutation in the Kinase domain of BCR-ABL and can have therapeutic indication. Also called as IRMA    |
| NA1003    | BCR-ABL Kinase Domain Mutations | 3-4 mL Bone marrow/ Peripheral Blood in EDTA (Lavender Top) Tube | 15 Days | Next Generation Sequencing            | Clinical history is mandatory, Old report number (if done from same lab) | Stable at 4°C for 72 hours. Transport in 2 to 8°C (with cold pack). |   |
| ME1000    | BCR-ABL Qualitative             | 3-4 mL Bone marrow/ Peripheral Blood in EDTA (Lavender Top) Tube | 3 Days  | Real Time Polymerase Chain Reaction   | Clinical history is mandatory, Old report number (if done from same lab) | Stable at 4°C for 72 hours. Transport in 2 to 8°C (with cold pack). | As a prognostic marker in ALL patients. Presence of BCR-ABL gene rearrangement is associated with poor prognosis. |

| Test Code | Test Name                                      | Sample Requirement   | TAT    | Method                              | Special Instructions   | Shipping & Stability Conditions                                     | Clinical Utility  |
|-----------|--|--|--------|-------------------------------------|--|---|---|
| ME1005    | BCR-ABL Quantitative with p210 breakpoint      | 3-4 mL Bone marrow/ Peripheral Blood in EDTA (Lavender Top) Tube   | 3 Days | Real Time Polymerase Chain Reaction | Clinical history is mandatory  | Stable at 4°C for 72 hours. Transport in 2 to 8°C (with cold pack). | confirms clinical diagnosis of Chronic Myeloid Leukemia (CML) patients to stratify patients for Imatinib therapy                                |
| ME1002    | BCR-ABL Quantitative, International Scale [IS] | 3-4 mL Bone marrow/ Peripheral Blood in EDTA (Lavender Top) Tube   | 3 Days | Real Time Polymerase Chain Reaction | Clinical history is mandatory, Old report number (if done from same lab) | Stable at 4°C for 72 hours. Transport in 2 to 8°C (with cold pack). | To confirm the diagnosis of CML & monitor the progress CML treatment  |
| YB1004    | BCR-ABL translocation [t(9:22)]                | Detection of mutation in the Kinase domain of BCR-ABL and can have therapeutic indication. Also called as IRMA | 5 days | Fluorescence In Situ Hybridization  | Brief Clinical history is mandatory                                      | Transport in 2 to 8°C (with cold pack) within 72 hrs.               | Help diagnose chronic myelogenous leukemia (CML) or a type of acute lymphoblastic leukemia (ALL) Monitor treatment Detect resistance to therapy |

# MYELOMA

## PLASMA CELL LYMPHOMA PANELS

Several mAbs such as daratumumab (anti-CD38), isatuximab (anti- CD38) and elotuzumab (anti-SLAMF7) and small molecules inhibitors such as first-in-class oral SINE selinexor, the oral proteasome inhibitor ixazomib and the BCL2 inhibitor venetoclax have shown activity in MM.

Daratumumab, initially approved as a single agent in 2015 for patients with R/R MM previously treated with a proteasome inhibitor and an immunomodulatory agent, was subsequently evaluated in different combinations including first-line regimens.

Although MM is still an incurable disease, there is no doubt that it is also a disease with a high number of active new treatments.

B-cell maturation antigen (BCMA) is a specific biomarker of normal and malignant plasma cells and has been regarded as a target for the development of new therapies in MM, including ADCs, CAR-T cells and bispecific T-cell engagers (BiTEs). Among them, belantamab mafodotin-blmf, a BCMA-targeted ADC, and idecabtagene vicleucel, a first-in-class BCMA CAR-T cell therapy, have been approved by the FDA for patients with MM after at least four prior lines of treatment. Although MM is still an incurable disease, there is no doubt that it is also a disease with a high number of active new treatments.

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| Test Code | Test Name                                   | Sample Requirement                              | TAT                                 | Method                | Shipping & Stability Conditions | Clinical Utility   |
|-----------|---|---|-------------------------------------|-----------------------|---------------------------------|--|
| YB1122    | COREprime Multiple Myeloma Diagnostic Panel | 3mL Serum from 1 SST, 3 mL EDTA ( Lavender Top) | Cut-off 11 AM, report same day 8 PM | Multiple Technologies | Ship refrigerated               | Kappa/lambda light chains, free ,immunofixation , Protien electrophoresis, Beta 2 microglobulin, CBC, BUN, Creatinine, Calcium, Albumin, LDH, Immunoglobulin profile |

Creatinine, CBC, BUN, Calcium, Albumin, LDH, Beta-2-Microglobulin, Protein Electrophoresis, Immunofixation Electrophoresis, Immunoglobulin IgG, Immunoglobulin IgA, Immunoglobulin IgM, Kappa Free Light Chain, Lambda Free Light Chain.

| Test Code | Test Name  | Components  | Sample Requirement  | TAT                            | Method                | Shipping & Stability Conditions  |
|-----------|--|---|---|--------------------------------|-----------------------|--|
| P00285    | Multiple Myeloma Comprehensive Panel Quantitative, Serum | Beta 2 Microglobulin, Protein Electrophoresis, Immunofixation Electrophoresis, Immunoglobulin Profile, Kappa/Lambda- Free light chain | 3mL Serum from 1 SST (Gel barrier tube). Separate Serum within 1 hour of collection | Sample by 1 pm report next day | Multiple Technologies | Room Temperature: 1 day, Refrigerated (2-8°C): 7 days, Frozen (-20°C): 30 days |

Immunofixation Electrophoresis can be used to identify abnormal bands in order to determine which type of antibody (immunoglobulin) is present. Immunofixation Quantitative Includes: Immunofixation Quantitative-Protein electrophoresis, Immunofixation, IgG, IgM, , freelite and Beta 2 microglobulin

| Test Code | Test Name  | Components  | Sample Requirement   | TAT                                  | Method                | Shipping & Stability Conditions |
|-----------|--|---|--|--------------------------------------|-----------------------|---------------------------------|
| VB1059    | Multiple Myeloma Comprehensive Panel Quantitative, Urine | Protein Electrophoresis, Immunofixation, Immunoglobulin Profile, Kappa/Lambda- Free light chain | 10 mL 24 Hrs Urine (Preferred) in Sterile Container without Preservatives, Spot Urine is also acceptable | Sample by Saturday, Report in 4 days | Multiple Technologies | Ship refrigerated or frozen     |

This assay is useful for diagnosing & monitoring patients with Monoclonal gammopathies. Protein electrophoresis alone is not considered an adequate screening test for Monoclonal gammopathies. immunofixation Quantitative.

| Test Code | Test Name                            | Components  | Sample Requirement   | TAT                            | Method                             | Shipping & Stability Conditions   | Clinical Utility  |
|-----------|--------------------------------------|---|--|--------------------------------|------------------------------------|---|---|
| YB1072    | Multiple Myeloma 7 Markers Panel     | del17p, t(14;20), Monosomy 1/ Chromosome 1 aberration, t(14;16), t(11;14), del13q and t(4;14)                 | 3-4 mL Bone marrow/Peripheral Blood in EDTA (Lavender Top), Sodium heparin (Green Top) Tube. | 5 Days                         | Fluorescence In Situ Hybridization | Transport in 2 to 8°C (with cold pack) within 72 hrs.                               | Prognostic marker in patients with Multiple myeloma.                          |
| WB1196    | Multiple Myeloma Flow Panel          |   | 3-4 mL Bone marrow/Peripheral Blood in EDTA (Lavender Top), Sodium Heparin (Green Top) Tube. | 2 Days                         | Flow Cytometry                     | Transport in 2 to 8°C (with cold pack). EDTA sample in 48 hrs and Heparin in 72 hrs | Prognostic Marker in Patients with Multiple Myeloma.                          |
| WB1144    | Multiple Myeloma MRD                 |   | 3-4 mL Bone marrow/Peripheral Blood in EDTA (Lavender Top), Sodium Heparin (Green Top) Tube. | 3 Days                         | Flow cytometry                     | Transport in 2 to 8°C (with cold pack).   | Estimation of Minimal Residual Disease in Diagnosed cases of Multiple Myeloma |
| P00687    | Multiple Myeloma, Diagnostic Panel-1 | Protein Electrophoresis, Immunofixation Electrophoresis, Kappa/Lambda- Free light chain, Beta-2-microglobulin | 3 mL (2 mL min.) serum from 1 SST.   | Sample by 1 pm report next day | Multiple Technologies              |   |   |
| P00688    | Multiple Myeloma, Diagnostic Panel-2 | Protein Electrophoresis, Immunofixation Electrophoresis, Kappa/Lambda- Free light chain, Beta-2-microglobulin | 3 mL (2 mL min.) serum from 1 SST.   | Sample by 1 pm report next day | Multiple Technologies              |   |   |

| Test Code | Test Name                                 | Components   | TAT    | TAT            | Method  | Shipping & Stability Conditions                       |
|-----------|---|--|--------|----------------|---|---|
| IA1187    | Kappa (Diagnosis of B-cell Lymphomas)     | Formalin fixed paraffin embedded tissue block  | 4 Days | IHC            | Transport at ambient (18-25°C)  | Diagnosis of B-cell lymphoma & Plasma cell Dyscrasism |
| AL1209    | Kappa and Lambda- Free Light Chain, Urine | 10 ml of Spot Urine (acceptable) or 10 ml of aliquot of 24 hour Urine sample (Preferred) | 4 Days | IHC            | Transport at 2 to 8°C (with cold pack).   |   |
| WB1187    | Kappa Light Chain                         | 3-4 mL Bone marrow/ Peripheral Blood in EDTA (Lavender Top)/ Heparin (Green Top) Tubes   | 2 Days | Flow Cytometry | Transport at 2 to 8°C (with cold pack). EDTA sample in 48 hrs and Heparin sample in 72 hrs                  | Clonal Restriction/B-Cell Maturity Marker             |
| AL2478    | Kappa- Free Light Chain, Serum            | 3 mL (2 mL min.) Serum from 1 SST.   | 2 Days | Turbidimetry   | Ship refrigerated or frozen. Room Temperature: 1 day, Refrigerated (2-8°C): 7 days, Frozen (-20°C): 30 days |   |
| P00292    | Kappa/Lambda-Free Light Chain, Serum      | 3 mL (2 mL min.) Serum from 1 SST.   | 2 Days | Turbidimetry   | Ship refrigerated or frozen. Room Temperature: 1 day, Refrigerated (2-8°C): 7 days, Frozen (-20°C): 30 days |   |

There are several targeted therapies for myeloma, including:

- 1. Proteasome inhibitors:** Drugs such as bortezomib, carfilzomib, and ixazomib target and inhibit the proteasome, a cellular complex responsible for breaking down proteins. By blocking the proteasome, these drugs can help kill myeloma cells and slow down the progression of the disease.
- 2. Immunomodulatory drugs (IMiDs):** Drugs like lenalidomide and pomalidomide enhance the immune system's ability to fight myeloma cells. They can also inhibit the growth of blood vessels that support the tumor.
- 3. Monoclonal antibodies:** Antibodies like daratumumab and elotuzumab specifically target proteins on the surface of myeloma cells, marking them for destruction by the immune system or directly killing the cells.
- 4. Histone deacetylase inhibitors:** Drugs such as panobinostat and vorinostat can modify the way genes are expressed in myeloma cells, leading to their death.
- 5. Targeted kinase inhibitors:** Certain drugs like ibrutinib and dasatinib venetoclax can block specific signaling pathways that are important for the survival and growth of myeloma cells.
- 6. CAR T-cell therapy:** Chimeric Antigen Receptor (CAR) T-cell therapy involves modifying a patient's own immune cells to express a receptor that recognizes a specific protein on myeloma cells. These modified T-cells are then infused back into the patient, where they can recognize and eliminate myeloma cells.

Table 4. New Combinations in MM.

| Drug  | Indication   | Approval             | Trial  | Primary Endpoint   |
|---|--|----------------------|--|--|
| Elotuzumab (Elo) + pomalidomide + dexamethasone (EloPd) | R/R >2 prior therapies (including lenalidomide and PI) | FDA 2019<br>EMA 2019 | ELOQUENT-3<br>Phase II<br>EloPd vs Pd<br>(NCT02654132)       | PFS: 10.3 mo (EloPd)<br>vs<br>4.7 mo (Pd)<br>ORR: 53% vs 26%                                 |
| Elotuzumab (Elo) + lenalidomide + dexamethasone (EloRd) | R/R >1 prior therapy                                   | FDA 2015<br>EMA 2016 | ELOQUENT-2<br>Phase III!<br>EloRd vs Rd<br>(NCT01239797)     | Median PFS: 19.4<br>(EloRd)<br>vs 14.9 (Rd)<br>ORR: 78.5% vs 65.5%                           |
| Isatuximab + carfilzomib + dexamethasone (IsaKd)        | R/R >1 prior therapy                                   | FDA 2021<br>EMA 2021 | IKEMA<br>Phase III<br>IsaKd vs Kd<br>(NCT03275285)           | Median PFS: NR<br>(IsaKd) vs<br>19.15 mo (Kd)  |
| Isatuximab + pomalidomide + dexamethasone (IsaPd)       | R/R >2 prior therapies (including lenalidomide and PI) | FDA 2020<br>EMA 2020 | ICARIA-MM<br>Phase III!<br>IsaPd vs Pd<br>(NCT02990338)      | PFS at median FU<br>(11.6 mo): 11.53 mo<br>(IsaPd) vs<br>6.47 mo (Pd)<br>ORR: 60.49 vs 35.3% |
| Ixazomib + lenalidomide + dexamethasone (IxaRd)         | R/R >1 prior therapy                                   | FDA 2015<br>EMA 2015 | TOURMALINE-MM1<br>Phase III!<br>IxaRd vs Rd<br>(NCT01564537) | PFS: 20.6 mo (IxaRd)<br>vs<br>14.7 mo (Rd)   |
| Carfilzomib + lenalidomide + dexamethasone (KRd)        | R/R >1 prior therapy                                   | FDA 2015<br>EMA 2015 | ASPIRE<br>Phase III<br>KRd vs Rd<br>(NCT01080391)            | Median PFS: 26.3 mo<br>(KRd) vs 17.6 mo (Rd)   |
| Selinexor + bortezomib + dexamethasone (SVS)            | R/R >1 prior therapy                                   | FDA 2020             | BOSTON<br>Phase III<br>SVS vs Vd<br>(NCT03110562)            | PFS: 13.9 mo (SVS) vs<br>9.5 mo (Vd)   |
| Idecabtagene vicleucel                                  | R/R >4 prior therapies                                 | FDA 2021             | KarMMa<br>Phase II<br>(NCT03361748)                          | Median PFS: 8.8 mo<br>ORR: 73% with 33% CR   |
| Belantamab  | R/R >4 prior therapies                                 | FDA 2020             | DREAMM-2<br>Phase II<br>(NCT03525678)                        | ORR: 31%<br>DoR:   |

Abbreviations: CR, complete response; DoR, duration of response; EMA, European Medicines Agency; FDA, Food and Drug Administration; FU, follow-up; Kd, carfilzomib, dexamethasone; MM, multiple myeloma; mo, months; NR, not reached;

ORR, overall response rate; Pd, pomalidomide and dexamethasone; PFS, progression-free survival; PI, proteasome inhibitor.

R/R: relapsed/refractory; Rd, lenalidomide and dexamethasone; Vd, bortezomib and dexamethasone.

# SALIVARY GLANDS / MUCO EPIDERMOID CA

| Test Code | Test Name | Components | TAT    | TAT | Method  | Shipping & Stability Conditions            | Clinical Utility   |
|-----------|-----------|------------|--------|-----|---|--|--|
| IA1870    | MUC 1     | FFPE block | 3 Days | IHC | Date and time of sample withdrawn, Detailed clinical history required       | Transport at Ambient (18-25°C) t           | Overexpression of MUC1 is often associated with colon, breast, ovarian, lung and pancreatic cancers. |
| IA1871    | MUC 2     | FFPE block | 4 Days | IHC | Clinical History, Histopathology Report,                                    | Transport at Ambient (18-25°C)             | Differential Diagnosis of Intestinal cancer.   |
| IA2189    | MUC 4     | FFPE block | 4 Days | IHC | Clinical history is mandatory.  | Transport at Ambient (18-25°C)             |  |
| IA1872    | MUC5AC    | FFPE block | 4 Days | IHC | Clinical History, Histopathology Report,                                    | Transport at Ambient (18-25°C)             | Differential Diagnosis of Gastric Cancer.  |
| IA1223    | p53       | FFPE block | 4 Days | IHC | Clinical History, Histopathology Report, Any Radiological Findings required | Transport at ambient (18-25°C) temperature | Prognostic Marker  |

## MUC5A MUCB in Low Grade

CRTC1/MAML2 fusion in a low-grade

HER2, EGFR or MUC1 MUC1, MUC2, MUC 4 are expressed more in high-grade tumors,

NOTCH1, PIK3CA, CDKN21, ERBB2, HER2,

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913015/>

## Oncogenes and Its Potential Therapeutic Targets in Treating Mucoepidermoid Carcinoma

Targeted agent      Oncogenes involved in MEC

Sorafenib              VEGF and ANG2

Nintedanib           VEGFR, FGFR, and PDGFR

Trastuzumab        HER2/neu

Lapatinib             EGFR and erbB2

ANA-12                TrkB and BDNF

MEC: mucoepidermoid carcinoma; VEGF: vascular endothelial growth factor; VEGFR: VEGF receptor; FGFR: fibroblast growth factor receptor; PDGFR: platelet-derived growth factor receptor; HER2/neu: human epidermal growth factor receptor 2; EGFR: epidermal growth factor receptor; erbB-2: receptor tyrosine-protein kinase; TrkB: tropomyosin receptor kinase B; BDNF: brain-derived neurotrophic factor.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9818327/>





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