



# Management of **solid tumours** in Biopathology





| Discipline                 | Affected organ / Tumours                                                                                           |                                                                                                                 | Immunohistochemistry                           | Molecular cytogenetics (FISH)                                                                                                                                                                                                                                                                                                                                                                                                               | Molecular biology                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Other relevant specialised medical pathology tests                                                                                                        |
|----------------------------|--------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Gynecology                 |  Breast                           |                                                                                                                 | OR / PR / HER2 / Ki67<br>PDL-1                 | HER2 amplification                                                                                                                                                                                                                                                                                                                                       | Somatic BRCA 1/2 <sup>(1)</sup> <br>PIK3CA <sup>(1)</sup> <br>PAM50 <sup>(1)</sup>                                                                                                                                                                                                                                                                                                                                              | HER2-serum <sup>(1)</sup><br>Evaluation of the risk of toxicity of fluoropyrimidines (5-FU)<br>CA 15-3 / ACE                                              |
|                            |  Ovary                            |                                                                                                                 | MMR (MLH1 / MSH2 / MSH6 / PMS2) / PDL-1        |                                                                                                                                                                                                                                                                                                                                                                                                                                             | Somatic BRCA 1/2 <sup>(1)</sup> <br>MSI <sup>(1)</sup> - MLH1 methylation <sup>(1)</sup>                                                                                                                                                                                                                                                                                                                                                                                                                           | CA 125 - HE4 (ROMA Score) / ACE / CA 19.9 / CA 72.4                                                                                                       |
|                            |  Uterus, cervix and endometrium   |                                                                                                                 | MMR (MLH1 / MSH2 / MSH6 / PMS2) / PDL-1        |                                                                                                                                                                                                                                                                                                                                                                                                                                             | MSI <sup>(1)</sup> - MLH1 methylation <sup>(1)</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | HPV / SCC / Cyfra 21.1 / CA 125 / ACE / CA 19.9                                                                                                           |
| Digestive system           |  Stomach and oesogastric junction |                                                                                                                 | HER2 / MMR (MLH1 / MSH2 / MSH6 / PMS2) / PDL-1 | HER2 amplification  / MET amplification - NTRK 1-2-3 rearrangement                                                                                                                                                                                                                                                                                       | MSI <sup>(1)</sup> - MLH1 methylation <sup>(1)</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Evaluation of the risk of toxicity of fluoropyrimidines (5-FU) / EBV                                                                                      |
|                            |  Stomach and small intestine      | GIST                                                                                                            | MMR (MLH1 / MSH2 / MSH6 / PMS2) / PDL-1        |                                                                                                                                                                                                                                                                                                                                                                                                                                             | <sup>NGS</sup> Panel: CKIT  - PDGFRA  - BRAF                                                                                                                                                                                                                                                                                                                                                                                    | Evaluation of the risk of toxicity of fluoropyrimidines (5-FU)                                                                                            |
|                            |  Colo-rectal                      |                                                                                                                 | MMR (MLH1 / MSH2 / MSH6 / PMS2) / PDL-1        | HER2 amplification  / MET amplification - NTRK 1-2-3 rearrangement                                                                                                                                                                                                                                                                                       | SEPTINE 9 / <sup>NGS</sup> Panel: AKT1 - ALK - BRAF  - CTNNB1 - EGFR - HER2  - FBXW7 - FGFR1 - FGFR2 - FGFR3 - KIT - KRAS  - MAP2K1 - MET - NRAS  - PDGFRA - PIK3CA - PTEN - SMAD4 - STK11 - TP53<br>MSI <sup>(1)</sup> - MLH1 methylation <sup>(1)</sup> | AFP / ACE / CA19-9<br>Pancreas: VIP / Gastrin / Glucagon<br>Liver: Type III procollagen<br>Evaluation of the risk of toxicity of fluoropyrimidines (5-FU) |
|                            |  Pancreas                         |                                                                                                                 |                                                | NTRK 1-2-3 rearrangement                                                                                                                                                                                                                                                                                                                                                                                                                    | Somatic BRCA 1/2 <sup>(1)</sup>  / MSI <sup>(1)</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                           |
| Pulmonology                |  Lung                             |                                                                                                                 | ALK / ROS1 / PDL-1                             | Rearrangement: ALK  / ROS1  / RET  / NTRK 1-2-3  / NRG1<br>Amplification: ALK, MET, HER2, FGFR1 | <sup>NGS</sup> Panel: AKT1 - ALK - BRAF  - DDR2 - EGFR  - HER2 - FGFR1 - FGFR2 - FGFR3 - KIT - KRAS - MAP2K1 - MET  - NRAS - PDGFRA - PIK3CA - PTEN - STK11 - TP53<br>Liquid biopsy : EGFR <sup>(1)</sup>                                                 | ProGRP / NSE / CYFRA 21 / SCC / ACE                                                                                                                       |
| Dermatology / Ophtalmology |  Skin/Eye                         | Melanoma                                                                                                        | PDL-1                                          | Monosomy 3 (Uveal melanoma)                                                                                                                                                                                                                                                                                                                                                                                                                 | <sup>NGS</sup> Panel: BRAF  - NRAS - CKIT                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                           |
| Musculoskeletal system     |  Bone and soft tissue            | Ewing's Sarcoma / Neuroectodermal Tumour primitive / Small desmoplastic tumour round cells / Clear cell sarcoma |                                                | EWSR1 rearrangement                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                           |
|                            |                                                                                                                    | Liposarcoma                                                                                                     |                                                | MDM2 amplification<br>DDIT3 rearrangement (CHOP)                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                           |
|                            |                                                                                                                    | Synovialosarcoma                                                                                                |                                                | SS18 Rearrangement (SYT)                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                           |
|                            |                                                                                                                    | Inflammatory myofibroblastic tumour                                                                             |                                                | ALK rearrangement                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                           |
|                            |                                                                                                                    | Rhabdomyosarcoma                                                                                                |                                                | FOXO1A rearrangement (FKHR)                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                           |
|                            |                                                                                                                    | Infantile fibrosarcoma                                                                                          |                                                | ETV6 rearrangement                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                           |
| Central Nervous System     |  Brain                          | Glioma                                                                                                          |                                                | 1p/19q co-deletion<br>p16 deletion / EGFR amplification                                                                                                                                                                                                                                                                                                                                                                                     | MGMT methylation <sup>(1)</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                           |
|                            |                                                                                                                    | Medulloblastoma                                                                                                 |                                                | NMYC amplification<br>CMYC amplification                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                           |
| Uro-Nephrology             |  Bladder                        |                                                                                                                 |                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                             | Non-invasive molecular test for bladder cancer monitoring                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                           |
|                            |  Prostate                       |                                                                                                                 | MMR (MLH1 / MSH2 / MSH6 / PMS2) / PDL-1        |                                                                                                                                                                                                                                                                                                                                                                                                                                             | Somatic BRCA 1/2 <sup>(1)</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | PSA                                                                                                                                                       |
|                            |  Testicle                       |                                                                                                                 |                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | hcG dimeric molecule (alpha + beta)<br>hCG - free beta chain - subunit                                                                                    |
| Endocrinology              |  Adrenal glands                 | Neuroblastoma                                                                                                   |                                                | NMYC amplification / 1p36 deletion                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Chromogranin A                                                                                                                                            |

Legend: (1) Subcontracted

 Companion diagnostics test for targeted therapy (with marketing approval or temporary marketing approval)

<sup>NGS</sup> NGS gene panel (tissue)



|                                                                                  | Pre-analytics                                                                                                                                                                                              |                     |                                                             |                               |                        | Required informations                                                                        | Test request form                                                                                                                                            |
|----------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|-------------------------------------------------------------|-------------------------------|------------------------|----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                  | Paraffin embedded block                                                                                                                                                                                    | Slides              | Extracted DNA                                               | Cell free DNA Collection tube | Frozen plasma aliquots | Other                                                                                        |                                                                                                                                                              |
| Molecular cytogenetics (FISH)                                                    | X                                                                                                                                                                                                          | 3 coated slides 4µm |                                                             |                               |                        |                                                                                              | Clinical data / Histological report / Type of fixer / Fixing time / Tissue analysis requested on :<br>► primary tumour (location)<br>► metastasis (location) |
| Molecular biology (tissue)                                                       | X                                                                                                                                                                                                          | 6 slides slides 5µm | - 30 ng minimum<br>- Extraction date<br>- DNA concentration |                               |                        | For MSI analysis: it is essential to join a healthy tissue block/slice with the tumour block | Histological report                                                                                                                                          |
| Molecular Biology on peripheral blood for circulating tumour DNA (liquid biopsy) |                                                                                                                                                                                                            |                     |                                                             | X                             | X                      |                                                                                              | Diagnosis? monitoring? Progression? Anteriority of an EGFR mutation ?                                                                                        |
| PROSIGNA™ PAM50 (prognostic gene signature assay)                                | X                                                                                                                                                                                                          | 6 slides 5µm        |                                                             |                               |                        |                                                                                              | Clinical data / Histological report / Type of fixer / Fixing time / Size of the tumour (cm) / Number of lymph node involved                                  |
| SEPTINE 9                                                                        |                                                                                                                                                                                                            |                     |                                                             |                               |                        | 2 x 3.5 ml frozen EDTA plasma Protocol - Ref. P21-INTGB                                      |                                                                                                                                                              |
| Non-invasive molecular test for bladder cancer monitoring                        |                                                                                                                                                                                                            |                     |                                                             |                               |                        | 5 ml urine Collection kit on demand - Ref. K7-INTGB                                          |                                                                                                                                                              |
| RNASeq / TMB                                                                     | Contact us: sales@ctie.eurofinseu.com                                                                                                                                                                      |                     |                                                             |                               |                        |                                                                                              |                                                                                                                                                              |
| Lymphoma                                                                         |                                                                                                                                                                                                            |                     |                                                             |                               |                        |                                                                                              | Hematologic Malignancies test request Form - Ref. B8-INTGB                                                                                                   |
| Other tests                                                                      | Find all the essential information (pre-analytic, required documents, turnaround time etc.) relating to each analysis on <a href="http://www.eurofins-biomnis.ie">www.eurofins-biomnis.ie</a> > test Guide |                     |                                                             |                               |                        |                                                                                              |                                                                                                                                                              |
| Immunohistochemistry                                                             | Eurofins Biomnis Ireland - Phone: 1800 303 349 - Email: sales@ctie.eurofinseu.com                                                                                                                          |                     |                                                             |                               |                        |                                                                                              |                                                                                                                                                              |

## Note

Three biopathology techniques can be used for the analysis of a biomarker for diagnostic, prognostic or theranostic purposes for solid tumours:

- **The ImmunoHistoChemistry (IHC) technique**, interpreted by an anatomopathologist, makes it possible to evaluate the level of expression of a protein (loss of expression or over-expression). It is evaluated as a percentage of cells or expression level (+, ++, +++).  
*Examples: HER2-IHC, PDL1-IHC, MMR-IHC.*
- **The fluorescence in situ hybridisation (FISH) technique** interpreted by a cytogeneticist or an anatomopathologist with an expertise in cytogenetics, highlights a loss (deletion), a gain (over-representation and amplification) or a rearrangement of a locus. Two other derived techniques can also be used: CISH (Chromogenic ISH) and SISH (Silver-ISH). Eurofins Biomnis has opted for an fluorescence technique (Gold standard).  
*Example: HER2 FISH, ALK FISH.*

The IHC and FISH techniques are carried out directly on a slide from a tissue block embedded in paraffin. (or on frozen tissue or on tissue apposition for the FISH technique).

- **Molecular biology techniques** are interpreted by a molecular biologist or an anatomopathologist with expertise in molecular biology. They can be performed on tissue or peripheral blood (liquid biopsy or circulating tumour DNA) and are initiated by DNA or RNA extraction. On tissue, a minimum percentage of 20% of tumour cells is essential for the proper performance of these techniques (a tumour infiltration check is systematically carried out by a Eurofins Biomnis pathologist) and the detection threshold of the technique used must be of the order of 5%. The techniques used routinely are varied: NGS (DNaseq and RNAseq), Sanger, RT-PCR, Fragment Analysis, Methyl-PCR, etc. NGS analysis allows several genes to be analysed in a single step.

NB: The quality of interpretation of a FISH or molecular biology test depends directly on the preanalytical conditions of the sample (ischaemia time, type of fixative and fixation time), the reagents used, the robustness of the molecular biology technique (e.g. amplicon or capture) and the expertise of the clinical pathologist or anatomopathologist.

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