







































# 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 / PDL-1	HER2 amplification 	Somatic BRCA 1/2 <sup>(1)</sup>  PIK3CA <sup>(1)</sup>  PAM50 <sup>(1)</sup>	HER2-serum <sup>(1)</sup> Evaluation of the risk of toxicity of fluoropyrimidines (5-FU) CA 15-3 / ACE
	 Ovary		MMR (MLH1 / MSH2 / MSH6 / PMS2) / PDL-1		Somatic BRCA 1/2 <sup>(1)</sup>  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		<b>NGS Panel: CKIT  - PDGFRA  - BRAF</b>	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	<b>SEPTINE 9 / NGS Panel: AKT1 - ALK - BRAF  - CTNNB1 - EGFR - HER2  - FBXW7 - FGFR1 - FGFR2 - FGFR3 - KIT - KRAS  - MAP2K1 - MET - NRAS  - PDGFRA - PIK3CA - PTEN - SMAD4 - STK11 - TP53</b> MSI <sup>(1)</sup> - MLH1 methylation <sup>(1)</sup>	AFP / ACE / CA19-9 Pancreas: VIP / Gastrin / Glucagon Liver: Type III procollagen 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 Amplification: ALK, MET, HER2, FGFR1	<b>NGS Panel: AKT1 - ALK - BRAF  - DDR2 - EGFR  - HER2 - FGFR1 - FGFR2 - FGFR3 - KIT - KRAS - MAP2K1 - MET  - NRAS - PDGFRA - PIK3CA - PTEN - STK11 - TP53</b> Liquid biopsy : EGFR <sup>(1)</sup> 	ProGRP / NSE / CYFRA 21 / SCC / ACE
Dermatology / Ophthalmology	 Skin/Eye	Melanoma	PDL-1	Monosomy 3 (Uveal melanoma)	<b>NGS Panel: BRAF  - NRAS - CKIT</b>	
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 DDIT3 rearrangement (CHOP)		
		Synovialosarcoma		SS18 Rearrangement (SYT)		
		Inflammatory myofibroblastic tumour		ALK rearrangement		
		Rhabdomyosarcoma		FOXO1A rearrangement (FKHR)		
Central Nervous System	 Brain	Glioma		1p/19q co-deletion p16 deletion / EGFR amplification	MGMT methylation <sup>(1)</sup>	
		Medulloblastoma		NMYC amplification 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) 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)

**NGS** 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	
<b>Molecular cytogenetics (FISH)</b>	X	3 coated slides 4µm						Clinical data / Histological report / Type of fixer / Fixing time / Tissue analysis requested on : ▶ primary tumour (location) ▶ metastasis (location)	Solid Tumours - test request form - Ref. B9-INTGB
<b>Molecular biology (tissue)</b>	X	6 slides slides 5µm	- 30 ng minimum - Extraction date - DNA concentration			For MSI analysis: it is essential to join a healthy tissue block/slice with the tumour block	Histological report		
<b>Molecular Biology on peripheral blood for circulating tumour DNA (liquid biopsy)</b>				X	X		Diagnosis? monitoring? Progression? Anteriority of an EGFR mutation ?		
<b>PROSIGNA™ PAM50 (prognostic gene signature assay)</b>	X	6 slides 5µm						Clinical data / Histological report / Type of fixer / Fixing time Size of the tumour (cm) / Number of lymph node involved	
<b>SEPTINE 9</b>						2 x 3.5 ml frozen EDTA plasma Protocol - Ref. P21-INTGB			
<b>Non-invasive molecular test for bladder cancer monitoring</b>						5 ml urine Collection kit on demand - Ref. K7-INTGB			
<b>RNASeq / TMB</b>	Contact us: <a href="mailto:international@biomnis.eurofinseu.com">international@biomnis.eurofinseu.com</a>								
<b>Lymphoma</b>								Hematologic Malignancies test request Form - Ref. B8-INTGB	
<b>Other tests</b>	Find all the essential information (pre-analytic, required documents, turnaround time etc.) relating to each analysis on <a href="http://www.eurofins-biomnis.com">www.eurofins-biomnis.com</a> > test Guide								
<b>Immunohistochemistry</b>	International Division - Tel.: +33(0)4 72 80 23 85 - Email: <a href="mailto:international@biomnis.eurofinseu.com">international@biomnis.eurofinseu.com</a>								

## Note

Three biopathology techniques can be used for the analysis of a biomarker for diagnostic, prognostic or therapeutic 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 a 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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