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Selecting the Most Appropriate Molecular Test for Your Patient

At LifeStrands Genomics, we provide several molecular test options for almost all cancer types. While this allows clinicians to select a suitable test for each patient, it can also prove challenging to determine the best option from many available choices. While it is tempting to select the test that includes the largest number of genes and offers screening for many types of biomarkers, it may not always be the most suitable test, or even possible, for every case besides being costly. Similarly, a test that does not screen for all important biomarkers for a particular cancer type might prove unhelpful. While selecting an appropriate molecular test may be beneficial for therapy selection or of a diagnostic/prognostic value, a wrong-chosen test may lead to missing crucial molecular information and inappropriate management.

Here are some considerations to think about when selecting a test:

Panel Selection

- Which test has all the genes that should be ideally screened for a particular case that would provide the best chance for actionable mutations being discovered without being wasteful?
- Has a basic molecular test been performed, and are you seeking more information to help the patient with further management or clinical trials/compassionate drug access? Or is this the first time sending the patient's sample for a molecular test?
- Is the molecular test requested because the patient has developed resistance to initial therapy?
- Is there an adequate amount of tissue available for a particular test? Or should you go for a smaller test panel for which the small amount of tissue may be adequate and still able to provide most of the information that might be useful?
- Are you confident that the genes of interest included in the chosen assay are covered adequately, and not just small foci of each gene (hotspots) are screened for and may not cover all the areas of interest?
- Is screening for fusions beneficial for a particular type of tumour? Or should you only consider testing for mutations (and copy number changes)? Or does the case demand a comprehensive genomic analysis that includes all types of genetic aberrations (mutations, copy number changes, fusions, MSI, TMB etc)? Please note that a 500-genes fusion panel will only screen for fusions and is not the same as a 500-genes comprehensive genomic analysis assay. For example, a fusion panel that includes *BRAF* will only screen for *BRAF* fusion, such as *BRAF-KIAA1549* fusion, which is prevalent in pilocytic astrocytoma. This assay will not screen for *BRAF V600E* mutation that is required for melanoma management.

Affordability and Turnaround Time

- Is the patient covered by any healthcare insurance that includes payouts that will cover the cost of the test?
- Is there any existing government reimbursement programme that will cover the cost of the test (fully or partially), or would the cost be borne by the patient?
- Do you need the results urgently within 2 – 4 days, or is it possible to wait for 10 days to 2 weeks for the report?

While it would be convenient to offer one option for each cancer type, if all factors mentioned above are considered, there would be more than one option requiring careful consideration depending on the circumstances.

This table features a list of OncoStrands® test recommendations for some cancer types.

Rows highlighted in lavender are primary recommendations. The rest are circumstantial based available options.

NON-SMALL CELL LUNG CANCER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Essential Combined (DNA +Fusion)**	**Mutations CNVs Fusions**	**Mutations** – *EGFR, KRAS, BRAF, NRAS, HER2* **CNVs** – *HER2, MET* **Fusions** – *ALK, ROS1, RET, NTRK1, NTRK2, NTRK3* **Others** - *MET* ex 14 skipping mutations
If only fusion testing is required (e.g. if initial *EGFR* testing has been done elsewhere or *ALK/ROS1* IHC shows strong staining).	**Essential Fusion**	**Fusions**	**Fusions** – *ALK, ROS1, RET, NTRK1, NTRK2, NTRK3* (and *MET* ex 14 skipping mutations)
If only mutations such as *EGFR, HER2, KRAS, BRAF* are required and not *ALK, ROS1, RET* fusions.	**Essential DNA**	**Mutations CNVs**	**Mutations** – *EGFR, KRAS, BRAF, NRAS, HER2* **CNVs** – *HER2*
If repeat testing is requested due to drug resistance.	**Essential Combined (DNA +Fusion)**	**Mutations CNVs Fusions**	Resistance to *EGFR TKI, ALK/ROS1* inhibitor; *TRK* inhibitor therapies is a usual phenomenon after a period of treatment. Resistance can develop due to various secondary mutations, CNVs or fusions. Repeat testing can provide valuable clues to the mechanism of resistance and may also guide further therapy. Hence a combined panel is recommended.
If further exploratory testing is sought for comprehensive analysis, including TMB when initial testing is unhelpful.	**Comprehensive**	**Mutations CNVs Fusions MSI TMB**	All the above-mentioned genes + TMB. Includes other genes relevant to potential clinical trials.
COLORECTAL CANCER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Essential DNA**	**Mutations CNVs**	**Mutations** – *EGFR, KRAS, BRAF, NRAS, HER2* **CNVs** – *HER2*
If MSI testing is required or in cases where MMR IHC is not done or not possible/preferred.	**Extended**	**Mutations CNVs MSI**	All the above-mentioned genes + Other relevant genes, including *MLH1, PMS2, MSH2, MSH6,* and *MUTYH.* Also provides **a highly accurate MSI status** (confirmatory MMR IHC testing is performed on all MSI unstable cases in our laboratory). Other genes of potential significance for clinical trials are also covered.
If MMR IHC (*MLH1, PMS2*) is abnormal.	**MLH1 Promoter Methylation**	**MLH1**	Only for MLH-1 promoter methylation testing.
STOMACH CANCER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Extended**	**Mutations CNVs MSI**	**Mutations** – *BRAF, RAS, HER2* **CNVs** – *HER2* **MSI** and other genes relevant for clinical trials.
If comprehensive genomic profiling is considered useful for the case and affordable.	**Comprehensive**	**Mutations CNVs Fusions MSI TMB**	All the above-mentioned genes + TMB. **Fusions** – *NTRK1, NTRK2, NTRK3* Includes other genes relevant to potential clinical trials.

MELANOMA			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Essential DNA**	**Mutations CNVs**	**Mutations** – *BRAF, NRAS, KIT, CDKN2A*
If further exploratory testing is required and affordable.	**Comprehensive**	**Mutations CNVs Fusions MSI TMB**	Besides all relevant mutations covered, the assay screens for TMB, which can be a useful biomarker in melanoma. NTRK fusions can also be found, albeit rarely in melanoma.
CHOLANGIOCARCINOMA			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**DNA 68 + Essential Fusion**	**Mutations CNVs Fusions**	**Mutations** – *IDH1, IDH2, FGFR, BRCA1, BRCA2* **CNVs** – *HER2* **Fusions** – *FGFR1, FGFR2, FGFR3, NTRK1, NTRK2, NTRK3*
If MSI testing is considered.	**Extended + Essential Fusion**	**Mutations CNVs Fusions MSI**	All the above-mentioned genes + **MSI status** Includes other genes relevant to potential clinical trials.
PROSTATE CANCER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Extended**	**Mutations CNVs MSI**	**Mutations** – *BRCA1, BRCA2* and several other relevant HRR genes with FDA-approved therapy, including *ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51, RAD54* **MSI**, and other genes for clinical trial eligibility.
If more comprehensive genomic profiling is considered suitable and affordable.	**Comprehensive**	**Mutations CNVs Fusions MSI TMB**	All the above-mentioned genes + TMB. **Fusions** – *NTRK1, NTRK2, NTRK3* Includes other genes relevant to potential clinical trials.
PANCREATIC CANCER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Extended**	**Mutations CNVs MSI**	**Mutations** – *BRCA1, BRCA2, BRAF, KRAS, HER2, PALB2* **CNVs** – *HER2* **MSI**, and other genes for clinical trials eligibility.
If more comprehensive genomic profiling is considered suitable and affordable.	**Comprehensive**	**Mutations CNVs Fusions MSI TMB**	All the above-mentioned genes + TMB. **Fusions** – *NTRK1, NTRK2, NTRK3* Includes other genes relevant to potential clinical trials.
OVARIAN CANCER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Extended**	**Mutations CNVs MSI**	**Mutations** – *BRCA1, BRCA2, BRAF, HER2* **CNVs** – *HER2* **MSI**, and other genes for clinical trials eligibility.
Note: HRD panel for ovarian cancer is currently being validated. This will be offered within the Comprehensive Panel as an option to add the test at extra cost. This HRD panel has been developed by Illumina in collaboration with Myriad (which is FDA approved HRD test, myChoiceCDx).			

ENDOMETRIAL CANCER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Extended**	**Mutations CNVs MSI**	**Mutations** – *POLE, TP53* **CNVs** – *HER2* **MSI**, and other genes for clinical trial eligibility.
BREAST CANCER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**DNA 68**	**Mutations CNVs**	**Mutations** – *BRCA1, BRCA2, PIK3CA, PALB2* **CNVs** – *HER2*, and Other genes for clinical trials eligibility.
If comprehensive genomic profiling is considered suitable and affordable.	**Comprehensive**	**Mutations CNVs Fusions MSI TMB**	All the above-mentioned genes + MSI & TMB. **Fusions** – *NTRK1, NTRK2, NTRK3* Includes other genes relevant to potential clinical trials.
THYROID LESIONS			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Essential Combined (DNA +Fusion)**	**Mutations CNVs Fusions**	**Mutations** – *BRAF, KRAS, NRAS, HRAS, RET* **Fusions** – *RET, NTRK1, NTRK2, NTRK3*
URINARY BLADDER			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Extended + Essential Fusion**	**Mutations CNVs Fusions MSI**	**Mutations** – *BRAF, FGFR1, FGFR2, FGFR3* **Fusions** - *FGFR2, NTRK1, NTRK2, NTRK3* **MSI**, and other genes for clinical trial eligibility.
If comprehensive genomic profiling is considered suitable and affordable.	**Comprehensive**	**Mutations CNVs Fusions MSI TMB**	All the above-mentioned genes + TMB. **Fusions** – *NTRK1, NTRK2, NTRK3* Includes other genes relevant to potential clinical trials.
GIST (GASTRO-INTESTINAL STROMAL TUMOUR)			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Essential DNA**	**Mutations CNVs**	**Mutations** – *KIT, PDGFRA*
SARCOMA			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Primary recommendation	**Comprehensive Fusion**	**Fusions**	501 fusion genes are covered, of which roughly 180 genes are useful for sarcoma screening. The assay also detects novel fusion partners. *NTRK* fusions for targeted therapy are also covered.
If testing also requires mutation screening (only required in very select cases).	**Comprehensive Fusion + DNA 68**	**Mutations Fusions**	In some spindle cell lesions, testing for mutations like *GNAS, CTNNB1* is clinically important.

BRAIN TUMOURS			
Circumstance(s)	**Recommendation(s)**	**What is covered?**	**Relevant genes/biomarkers covered + comments (if any)**
Only for *IDH* testing.	**Essential DNA**	**Mutations CNVs**	**Mutations** – *IDH1, IDH2* **CNVs** – *EGFR, CDKN2A/2B*
Glioma grading and *IDH* testing.	**DNA 68**	**Mutations CNVs**	**Mutations** – *IDH1, IDH2, TERT, BRAF* **CNVs** – *EGFR, CDKN2A/2B*
For glioma grading and *IDH* testing, and therapy.	**DNA 68 + Essential Fusion**	**Mutations CNVs Fusions**	**Mutations** – *IDH1, IDH2, TERT, BRAF* **CNVs** – *EGFR, CDKN2A/2B* **Fusions** – *NTRK1, NTRK2, NTRK3*
For pilocytic astrocytoma.	**Essential Combined (DNA +Fusion)**	**Mutations CNVs Fusions**	**Mutations** – *IDH1, IDH2, TERT, BRAF* **CNVs** – *EGFR, CDKN2A/2B* **Fusions** – *BRAF*
For pilocytic astrocytoma, if only BRAF fusion testing is required.	**Essential Fusion**	**Fusions**	**Fusions** – *BRAF*
For midline and some other types of gliomas.	**Extended**	**Mutations CNVs**	**Mutations** – *H3K27M, H3F3, HIST1H*
For NTRK and other fusion testing in paediatric glioma.	**Comprehensive Fusion**	**Fusions**	**Fusions** – *NTRK1, NTRK2, NTRK3* and many other relevant fusions
Glioblastoma requiring MGMT testing.	**MGMT Promoter Methylation**	**MGMT**	Only for MGMT promoter methylation testing.
Note: A dedicated brain tumour panel with a wide coverage of many tumour types is being validated for both adults and paediatric. To be offered soon.			

The following OncoStrands® tests are mentioned in the recommendations above:

NGS for Tissue Biopsy

- Essential Combined (50 genes, screens for mutations, CNVs and fusions)
- Essential DNA (45 genes, detects mutations and CNVs)
- Essential Fusion (18 genes, fusion only)
- DNA 68 (68 genes, detects mutations and CNVs)
- Extended (109 genes for mutations, CNVs and MSI)
- Comprehensive Fusion (Illumina TruSight RNA 501 genes) - only screens for fusions
- Comprehensive (Illumina TSO500 panel, 523 genes) – for comprehensive analysis that includes mutations, CNVs, MSI, and TMB. Also includes fusion testing for 55 out of the included 523 genes.

Other Tests

- MGMT promoter methylation
- MLH-1 promoter methylation

Please contact us to discuss other testing options for other tumour types or scenarios not included in the list above. For more information on how to order the test, please contact us at enquiry@lifestrandsgx.com or visit our website at www.lifestrandgx.com.