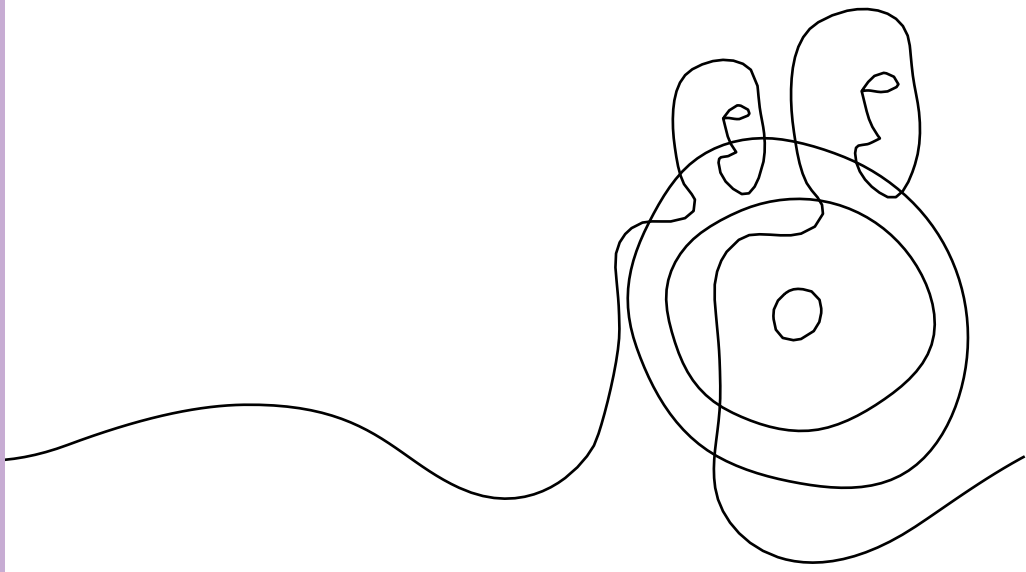
# Com.Pl.i.t DX

**Personalised treatment based on tumour biology**

For patients with lung, colorectal and breast cancer



"Your genes speak, we translate"

Genekor

Committed to Biotechnological Innovation

# Com.Pl.i.t DX®

**Com.Pl.i.t DX®** polygenic tests provide valuable information that can be used to select the optimal targeted therapy for patients. By analyzing multiple genes simultaneously, they provide a detailed fingerprint of the tumor biology, which is used by the treating physician to **personalize the** patient's **treatment plan.**

**Com.Pl.i.t DX®** are essential for the individualization of the treatment plan.

- Identify the molecular profile of the tumour such as gene mutations and copy number variations for inoperable tumours
- Specify the indicated drugs that target the mutated gene(s) or the pathway in which the genes are involved
- Identify the mutations associated with resistance to targeted therapy
- Recommend off-label treatments and/or suggest treatments that are currently in clinical trials

**Com.Pl.i.t DX®** tests are designed to offer maximum sensitivity and specificity.

All findings are categorized using the most reliable and upgraded databases and *in silico* analysis algorithms. Gene rearrangement analysis is also included. The combination of these provides comprehensive and reliable information to patients and physicians.

## Why are Com.Pl.i.t DX® polygenic tests the best tool for selecting the optimal personalised treatment?

- **They offer reliable information**

Advanced Next Generation Sequencing technology, also known as NGS, is used to fully analyse a panel of genes associated with targeted and personalised therapy. Also included in **Com.Pl.i.t DX®** is the analysis of gene rearrangements, providing comprehensive and reliable information to the patient and the treating physician. The molecular profile of each patient's tumor enables us to provide a highly personalized treatment option.

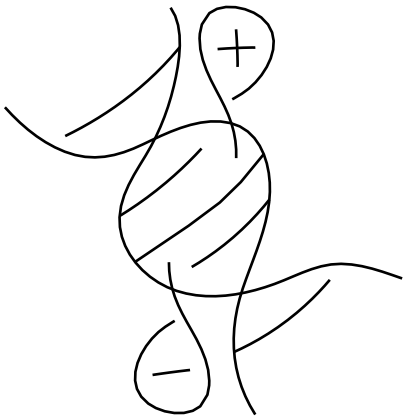
- **Time, Sample and Cost Savings**

The great advantage of the **Com.Pl.i.t DX®** multigene test is that it uses a minimal tumour sample, in which all cancer-related genes are analysed simultaneously, providing a clear and comprehensive answer quickly and at a lower cost. This is the most reliable solution, unlike single-gene tests, which use a larger sample volume and/or additional samples, increasing time and cost while missing important genes in the process.

- **Continuous support to patient and doctor from our specialized team**

Direct access to scientific and procedural support, as well as to useful information, is very important. We know this and provide continuous support to the doctor and the patient through our customer service department and our scientific advisors, who have the knowledge and expertise to always support the doctors' work in the best possible way.

*Next Generation Sequencing (NGS) technology is used to analyse several gene mutations in the same sample simultaneously, saving valuable material.*



# Com.Pl.i.t DX® Lung

**Com.Pl.i.t DX® Lung** is designed to help the treating physician choose what is the optimal treatment based on the tumor biology of the Non-Small Cell Lung Cancer patient.

## Gene Table

| ***Mutations in 27 Genes*** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *ACT1* | *ALK* | *BRAF* | *CDKN2A* | *CTNNB1* | *DDR2* | *EGFR* | *ERBB2* | *FBXW7* | *FGFR1* |
| *FGFR2* | *FGFR3* | *HRAS* | *KEAP* | *KRAS* | *MAP2K1* | *MET** | *NOTCH1* | *NRAS* | *PIK3CA* |
| *POLE* | *PTEN* | *RET* | *SMAD4* | *SMARCA4* | *STK11* | *TP53* | | | |
| ** The analysis includes MET amplifcation & to MET exon 14 skipping (DNA & RNA sequencing)* | | | | | | | | | |

| ***6 Gene rearrangements*** | | | | | | | |
|---|---|---|---|---|---|---|---|
| *ALK* | *ROS1* | *RET* | *NTRK1* | *NTRK2* | *NTRK3* | | |

| ***Immunotherapy*** | | | | | | | |
|---|---|---|---|---|---|---|---|
| *PD-L1* | | | | | | | |

*KEAP1, SMARCA4* and *CDKN2A* genes were added to the new **Com.Pl.i.t DX® Lung**:

- Patients with NSCLC with *STK11* and *KEAP1* mutations have a worse prognosis. These mutations especially in *KRAS* mutated tumors are associated with lower efficacy of immunotherapy (PMID: 34740862).
- Patients with NSCLC and *SMARCA4* mutations, despite their unfavourable prognosis, seem to benefit from immunotherapy or the combination of immunotherapy and chemotherapy. The coexistence of *SMARCA4* and mutations in other genes, including *KRAS, KEAP1, STK11* and *PBRM1,* may result in a reduced response to ICI immunotherapy.
- Multi-treated patients with NSCLC with a loss or mutation in the *CDKN2A* gene had a modest response to palbociclib monotherapy. In addition, loss of *CDKN2A* function has been associated with resistance to immunotherapy in MMC (PMID: 34625620)

With the addition of the above genes, **Com.Pl.i.t DX® Lung** represents a complete molecular profile for patients with NSCLC with prognostic and especially predictive value, using the correct methodology according to the guidelines for the 9 approved targeted therapies:

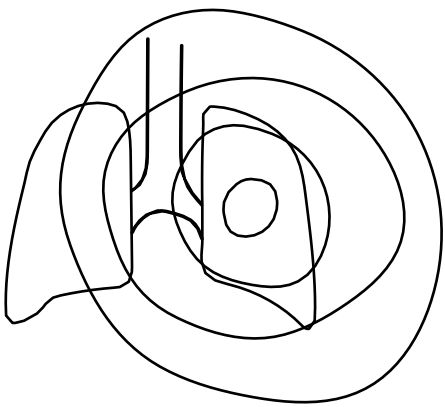
*EGFR, BRAFV600E, KRASG12C, ERBB2* (DNA sequencing)

*ALK, ROS1, RET, NTRK1,2,3* (RNA sequencing)

*MET* exon 14 skipping mutation (DNA & RNA sequencing)

*Sample: Tissue Enclosed in Paraffin Tissue*

*Result Time: 10 working days*



# Com.Pl.i.t DX® Colon

**Com.Pl.i.t DX® Colon** is designed to help the treating physician choose what is the optimal treatment based on tumor biology in metastatic colorectal cancer.

In colorectal cancer, somatic mutations are detected in genes involved in pathways related to the pathophysiology and treatment of cancer.

## Approved targeted therapies associated with several genes

***KRAS & NRAS*** genes: commonly used to identify colorectal cancer patients who are unlikely to benefit from *anti-EGFR* therapy. Approximately 50% of colorectal cancer tumours carry mutations in one of these genes.

***BRAF*** gene: Involved in the RAS/RAF/MEK/ERK pathway. This gene has an approved therapy for the V600E mutation, which is detected in approximately 10% of patients.

There is also an approved treatment for ***HER2*** gene amplification in patients with tumours without mutations in the ***KRAS, NRAS*** genes. In these cases, ***HER2*** analysis is performed using the FISH technique, as recommended by international guidelines.

In addition, approved biomarkers that are associated with targeted therapy, regardless of cancer type, can be detected in a significant proportion of patients. Microsatellite instability (MSI) is an excellent marker of response to immunotherapy with immune checkpoint inhibitors.

Finally, there are approved treatments for rearrangements in the ***NTRK1, NTRK2 and NTRK2*** genes
and ***NTRK3***, as well as the ***RET*** gene.

Based on the large number of approved biomarkers for this cancer type, and the biomarkers currently under investigation in clinical trials, guidelines (NCCN, ESMO, ASCO) recommend the use of NGS multigene analyses, which offer faster and more complete information than the analysis of one or a few biomarkers.

## Gene table

| ***Mutations in 27 Genes*** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *ACT1* | *ALK* | *BRAF* | *CDKN2A* | *CTNNB1* | *DDR2* | *EGFR* | *ERBB2* | *FBXW7* | *FGFR1* |
| *FGFR2* | *FGFR3* | *HRAS* | *KEAP* | *KRAS* | *MAP2K1* | *MET** | *NOTCH1* | *NRAS* | *PIK3CA* |
| *POLE* | *PTEN* | *RET* | *SMAD4* | *SMARCA4* | *STK11* | *TP53* | | | |
| ** The analysis includes MET amplifcation & to MET exon 14 skipping (DNA & RNA sequencing)* | | | | | | | | | |

| ***6 Gene rearrangements*** | | | | | | | |
|---|---|---|---|---|---|---|---|
| *ALK* | *ROS1* | *RET* | *NTRK1* | *NTRK2* | *NTRK3* | | |

| ***Immunotherapy*** | | | | | | | |
|---|---|---|---|---|---|---|---|
| *MSI* | | | | | | | |

*Sample: Tissue Enclosed in Paraffin Tissue*

*Result Time: 12 working days*

# Com.Pl.i.t DX® Liquid

**Com.Pl.i.t DX® Liquid** analysis provides valuable information that can be used to select the optimal targeted treatment for patients. By analyzing multiple genes simultaneously, it provides a detailed fingerprint of the tumor biology, which is used by the treating physician to personalize the patient's treatment plan.

## Gene table

| ***Mutations in 12 genes*** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *ALK* | *BRAF* | *EGFR* | *ERBB2* | *KRAS* | *MAP2K1* | *MET* | *NRAS* | *PIK3CA* | *RET* |
| *ROS1* | *TP53* | | | | | | | | |

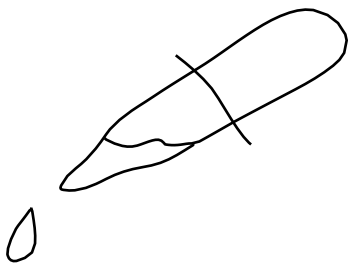
| ***3 Gene rearrangements*** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *ALK* | *ROS1* | *RET* | | | | | | | |

- A quantity of blood is taken from the patient, as in a routine blood test
- Isolation of cancer DNA and RNA detected in the blood, also known as free circulating cancer DNA and RNA
- Ability to detect mutations at very low rates (<1%)
- Advanced Next Gen- eration Sequencing (NGS) technology is used
- Each genetic position is read over 10,000 times by the NGS system
- Specialised software is used to analyse the data and convert raw data into information of practical use

**Com.Pl.i.t DX® Liquid is designed for patients with bowel or lung cancer.**

*Sample: Blood in 1 vial 10ml Cell-Free DNA BCT STRECK*

*10 working days*



# Com.Pl.i.t DX® Liquid Breast

**The Com.Pl.i.t DX® Liquid Breast** test is designed for postmenopausal women with recurrent or metastatic ER+/HER2- breast cancer and is a strong indicator of whether a patient should undergo specific targeted therapies.

## The Com.Pl.i.t DX® Liquid Breast Test is suitable for:

- Patients with breast cancer, with inoperable tumours and patients with limited or insufficient tissue biopsy material.
- Patients with multiple metastases.
- Patients on treatment or after completion of treatment. In this case, it gives an insight into the possible emergence of new targeted or resistance mutations to the therapy used.

## The test is highly recommended for targeted treatment decisions for:

- Postmenopausal women with advanced or metastatic ER+/HER2- breast cancer after relapse to previous treatment to decide on Elacestrant treatment based on *ESR1* gene mutations.
- Postmenopausal women with advanced or metastatic ER+/HER2- breast cancer after recurrence on previous treatment to decide on Alpelisib treatment based on *PIK3CA* gene mutations.
- Postmenopausal women with advanced or metastatic breast cancer after recurrence of previous treatment, in order to decide on treatments outside of indication or clinical trials.

## Gene Table

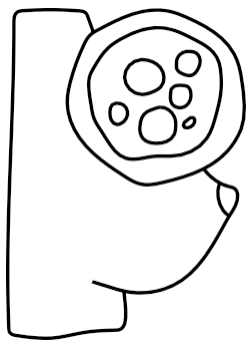
| ***Hotspot genes (appr. 152 hotsports)*** | *ACT1* | *EGFR* | *ERBB2* | *ERBB3* | *ESR1* | *FBXW7* | *KRAS* | *PIK3CA* | *SF3B1* | *TP53* |
|---|---|---|---|---|---|---|---|---|---|---|

| ***Copy number genes (CNVs)*** | *CCND1* | *ERBB2* | *FGFR1* |
|---|---|---|---|
| ***Full length genes*** | *TP53* | | |

- In the above gene panel, we detect mutations in the ***ESR1*** gene, which develop as a mechanism of resistance to hormonal therapy and are associated with approved therapy. (25-30%, based on international literature)
- We also detect the mutations in the ***PIC3CA*** gene**,** which are associated with an approved treatment. (incidence 35-45 % based on international literature)
- Finally, mutations are detected in other genes associated with experimental and off-label treatments.

*Sample: Blood in 1 vial 10ml Cell-Free DNA BCT STRECK*

*10 working days*



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