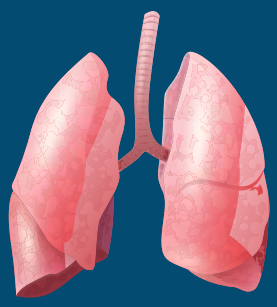
OncoDNA
THE CANCER THERANOSTIC COMPANY

SCREEN MORE THAN THE USUAL SUSPECTS IN

Non-Small Cell Lung Cancer



CLINICAL EVIDENCE FOR MOLECULAR PROFILING

A unique **combination of power** for decision making

Clinical evidence for molecular profiling in advanced non-small cell lung cancer

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer and a tumor eligible for a broad spectrum of targeted therapies already available or in clinical trials. Molecular profiling of the patient specific tumor using next generation sequencing (NGS) technology has become a key tool for facilitating treatment decisions and the clinical management of NSCLC patients. [1]

Managing Metastatic NSCLC With Rapid Progression:
Benjamin P. Levy: (Johns Hopkins Sidney Kimmel Cancer Center)
"At the very minimum, they need to test for EGFR, ALK, ROS, and BRAF. Those are the approved biomarkers, or actionable mutations, but I would argue that you should do comprehensive genomic profiling" [2]

As mentioned in the ESMO NSCLC guidelines: after morphological diagnosis, the next consideration is therapy-predictive biomarker testing with a wide panel of targetable alterations.

CLINICAL EVIDENCE OF COMPREHENSIVE GENOMIC PROFILING BEYOND THE USUAL SUSPECTS

• Tumor Mutational Burden & nivolumab + ipilimumab PF Survival
In patients with NSCLC and a high tumor mutational burden (TMB), irrespective of PD-L1 expression levels, progression-free survival was significantly longer with first-line nivolumab plus ipilimumab than with chemotherapy [3]

• MSI (Microsatellite instability) & Pembrolizumab FDA approved biomarker
Pembrolizumab is indicated for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) tumors (Keytruda Prescribing Information)[4]

• KRAS & EGFR TKI's (tyrosine kinase inhibitors) predictors
KRAS mutations are negative predictors of response to the EGFR TKI's, erlotinib, gefitinib, afatinib and osimertinib [5]

• STK11 inactivation and Immunotherapy resistance
Precision immunotherapy will require tailoring to the co-mutation status of individual tumors[6] .For example mutational inactivation of STK11/LKB1 represents a novel genomic predictor of de novo resistance to immune checkpoint blockade in KRAS-mutant LUAC, whereas TP53 co-mutations are associated with a high likelihood of response [6]

• RET rearrangement & response/PFS benefits
Benefit in terms of response (16%–47%) and progression-free survival (2–7months) with RET-selective inhibitors[7]

• ROS1 Mutations – a new standard biomarker
ROS-1 rearrangement is a standard biomarker in many countries, and several ALK inhibitors including crizotinib show activity in these patients[8]

• And much more...

Combining different molecular profiling assays **is the key to maximising the clinical benefit** of the treatment

A lot more
than the **usual**
hospitals routine...

Only OncoDNA can combine all this information in solid & liquid biopsies

- → **Improving treatment accuracy in comparison to NGS alone**
- → **Easing the physician adherence to recommendations**
- → **Improving significantly OS (overall survival)[10]**

GENES AND GENES REGION FOR SOLID AND LIQUID BIOPSIES

• EGFR-TKI's
erlotinib, gefitinib, afatinib, osimertinib, dacomitinib, ...
EGFR · KRAS · MET · ERBB2

• RET inhibitors
cabozantinib, vandetanib, ...
RET

• ALK inhibitors
crizotinib, alectinib, ceritinib, brigatinib, ...
ALK · ROS1

• MET ex14
cabozantinib, ...
MET

• BRAF + MEK inhibitors
vemurafenib, encorafenib, dabrafenib, trametinib, cobimetinib, ...
BRAF · MAP2K1 · MAP2K2

• Taxanes
docetaxel, paclitaxel, ...
TUBB3

• Anti metabolites Pyrimidic
gemcitabine, ...
RRM1

• Folic Acid Pathway/5FU
pemetrexed, ...
TS

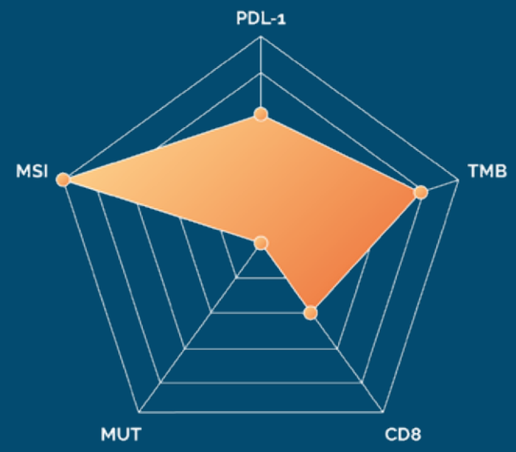
• Immune checkpoint inhibitors
pembrolizumab, atezolizumab, nivolumab, durvalumab, ...
Tumor Burden · MSI · PD-L1 · CD8 · MUTATIONS*

MUTATIONS: ARID2, B2M, BRD7, JAK1, JAK2, MLH1, MSH2, MSH3, MSH6, PBRM1, PD-1, POLD1, POLE, PMS2, PTEN, STK11

: Usual hospital routine · DNA/RNA · : Protein

A comprehensive test to give you a **clear and more precise** vision

An unique Immunogram to select the best treatment



CLINICAL RESPONSE

Our immunogram is created based on 5 key points, **PD-L1** % (FDA)[11], **TMB** (ASCO 2017)[12], **CD8** T-cell infiltrate (ASCO 2017), **MSI**(FDA) [14] and **Sensitivity/Resistance mutations** (ASCO 2017)[13]. With these tools, we are able to give you a clear vision of the potential clinical response of your patient.

The best combination of profiling on the market for

- → **The most comprehensive approach to characterise ICP (immune checkpoint) inhibitor treated patients.**
- → **Multifactor and integrative approach with a single partner.**
- → **The right molecular profiling combination for ICP**

5 PARAMETERS IMMUNOGRAM

1. **Expression of PD-L1**
   This is the first FDA approved biomarker. Although several antibodies exist to detect PD-L1 expression, only PD-L1 IHC 22C3 pharmDx (Dako) is approved as a companion diagnostic for pembrolizumab. Dako's PD-L1 IHC 28-8 pharmDx is approved as a complementary diagnostic for nivolumab. These two antibodies and others are available at OncoDNA.

2. **CD8 T-cell infiltrate as detected by IHC**
   The presence of CD8+ lymphocytes has been associated with better clinical outcomes for patients treated with ICP inhibitors.

3. **Tumor mutational burden (TMB)**
   TMB is a measurement of the mutations carried by tumor cells (number of mutations by units of coding area) and it correlates with higher level of neoantigens. High TMB has been associated with better response and increased survival rate for patients treated with ICP inhibitors.

4. **Microsatellite instability (MSI)**
   MSI, a type of genomic instability, is characterised by gains or losses of nucleotides from microsatellite tracts. It results from impaired DNA mismatch repair (MMR) and MSI-H(igh) status has been associated with high response rates and survival benefit for patients treated with checkpoint inhibitors.

5. **Mutations associated with sensitivity or resistance to ICP inhibitors**
   Mutations associated with sensitivity (e.g. POLE inactivating mutations) or resistance (e.g. STK11 inactivating mutations) to ICP inhibitors. We can test this continuously growing number of variants associated with an impact on immunotherapy.

Which OncoDNA solutions?

We use a combination of the most relevant molecular technologies to support oncologists in their decisions for patient treatment.

Our innovative approach is to combine next-generation sequencing (NGS) with immunohistochemistry (IHC) and additional techniques. This gives a comprehensive view of the tumor profile at the DNA, RNA and protein levels and can help identify more therapeutic options for the patient. Moreover, in 2016 we included liquid biopsy analyses in our solution portfolio, either in combination with solid biopsies or as standalone.

SOLID BIOPSY:

OncoDEEP®

COST-EFFECTIVE SOLUTION COMBINING DNA, RNA AND PROTEIN ANALYSIS OF A TISSUE SAMPLE

OncoDEEP analyses solid biopsies by combining next-generation sequencing (313 genes), IHCs to study protein expression and additional tests. This complete tumor profiling allows to predict patient response to approved or experimental targeted drugs, immunotherapies and chemotherapies.

The NGS panel is accurately designed according to oncologists' needs in their current practice. Importantly, it also includes an accurate determination of MSI, TMB and LOH. The NGS panel is regularly updated based on new findings reported in literature in order to provide patients with the most cost-effective solution.

MATERIAL

- 1 block or 25 slides (5 µm on SuperFrost Plus)

RECOMMENDED FOR :

- All solid tumors (stage III or IV) in adults
- Glioblastoma in children

SOLID AND LIQUID BIOPSIES:

OncoSTRAT&GO

THE MAIN SOLUTION IN NSCLC

THE COMPLETE SOLUTION INTEGRATING THE ANALYSIS OF SOLID AND LIQUID BIOPSIES

OncoSTRAT&GO is an integrated approach that combines the analyses of a solid biopsy (by next-generation sequencing (313 genes), IHCs and additional tests) with the analysis of a blood biopsy. The blood profiling focuses either on the circulating tumor DNA (for deciphering tumor heterogeneity) or in DNA from blood cells (for studying specific germline gene alterations related to BRCAness phenotype that are challenging to detect in FFPE samples).

OncoSTRAT&GO establishes a complete genetic profile of the tumor, which can be used to identify sensitivity or resistance to targeted therapies, chemotherapies and immunotherapies.

MATERIAL

- 1 blood sample (1x10 ml Streck tube or 1x10 ml EDTA tube)
- 1 block or 25 slides (5 µm on SuperFrost Plus)

RECOMMENDED FOR :

The following stage IV solid tumors in adults:

- **Non-small cell lung cancer**
- HR+, HER2+ and triple-negative breast cancer
- Colorectal cancer
- CUP
- Ovarian cancer
- Pancreatic cancer

NO SOLID BIOPSY:

OncoSELECT®

CANCER-SPECIFIC SOLUTION FROM A LIQUID BIOPSY SAMPLE

OncoSELECT is a fast and minimally invasive analysis of circulating tumor DNA from a blood sample.

It is the perfect solution to identify therapeutic options for cancer patients not able to have their tumor biopsied or whose biopsy is too old. It can be used as a tool to detect treatment resistance to targeted therapies (before first-line to check the heterogeneity of the disease, or during/after treatment to check for acquired resistance mutations), as well as for monitoring cancer progression.

MATERIAL

- 2 blood samples (2x10 ml Streck tubes)

RECOMMENDED FOR :

The following metastatic solid tumors in adults:

- Non-small cell lung cancer
- Breast cancer HR+ or HER2+
- Colorectal cancer

MONITORING RESPONSE:

OncoDNA can also provide other kinds of monitoring tools according to cancer type.

Do not hesitate to request more information or our support at **sales@oncodna.com**

Update of our solid panel part !

Our solid panel used alone (OncoDEEP) or in the mixed liquid/solid solution (OncoSTRAT&GO) is the most comprehensive profiling for solid tumor combining DNA and proteins data.

The solid panel profiles solid tumor samples by **sequencing** an extensive variety of genes linked to approved targeted therapies, combined with **IHC** tests to detect important **proteins** and with other tests, such as **MSI**, **gene fusion** and promoter methylation. The NGS panel is based on an accurate analysis of oncologists' needs in their current practice when the choice of solutions is reduced for the patients. The panel is updated every year based on advances reported in literature, so as to provide patients with the most economical and effective solutions. **The solid panel** provides information about approved or in development hormonal therapies, immunotherapies (through a personalized immunogram) and chemotherapy, as well as targeted therapies.

The best combination of profiling on the market for

→ **Immunotherapy**
→ **Targeted therapy**
→ **Chemotherapy**

} **selection**

WHAT IS NEW?

- 4x more genes and gene regions (313) for more acurate immunotherapy selection
- Broader microsatellite instability (MSI) and tumor mutational burden (TMB) coverage to increase the accuracy of our algorithm
- SNP: The most powerful panel for the best immunotherapy selection
- Broader fusion panel detection. Beyond the usual suspects

How to order a test?

1 1. LOGIN TO OncoSHARE by OncoDNA

OncoSHARE: An easy way to access & order your tests and receive the personalised report on treatment recommendation

When you join **OncoSHARE**, you become a member of an active network gathering together more than 13 000 patients and oncologists.

Regardless of whether information concerns patient health or payment, we take every precaution to ensure your security. OncoSHARE is used by oncologists to order our solutions, display interactive analysis reports and connect health care professionals to each other and to our team of experts.

In a simple, interactive manner, **OncoSHARE** will guide you in your selection of the most appropriate treatment options based on the unique signature of your patient's tumor.

www.oncoshare.com

2 2. ORDERING AN ONCODNA SOLUTION

2.1 Mention the person to bill - (credit card or wire transfer possible)
2.2 Select the kit you want to use and if we need to ship it to you
2.3 Describe the clinical state of your patient
2.4 We ship the corresponding sample collection kit to you

3 3. COLLECT THE SAMPLE

Send the kit back to OncoDNA (free of charge). Please print your own prepaid shipping label generated online at https://delivery.oncodna.com.

4 4. SAMPLE ANALYSIS

Upon arrival at the OncoDNA facilities, the sample quality is checked and the sample is recorded in our tracking system for further analysis.

5 5. YOUR REPORT READY ON ONCOSHARE

After interpretation by our experts, the results are published in an interactive report which is made available to you through your OncoSHARE account.

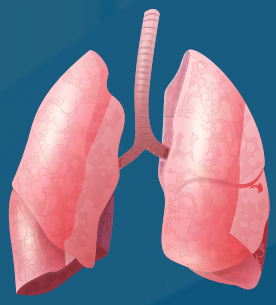
6 6. WE SUPPORT YOU

Support is available at all times, for patients through our Patient Care department **(infos@oncodna.com)** and for oncologists via our scientific team **(molecular@oncodna.com).**

OncoDNA
THE CANCER THERANOSTIC COMPANY

SCREEN MORE THAN THE USUAL SUSPECTS IN

Non-Small Cell Lung Cancer



CLINICAL EVIDENCE FOR MOLECULAR PROFILING

A unique **combination of power** for decision making

ONCODNA'S SOLUTION CAN ALSO BE OF HELP WITH MANY OTHER CANCER TYPES :

HEAD & NECK • BLADDER • PROSTATE • CANCER OF UNKNOWN PRIMARY • COLORECTAL • BREAST • MELANOMA • ...

REFERENCES :

__1.__Tsoulos N et al 2017 Tumor molecular profiling of NSCLC patients using next generation sequencing Oncol Rep. 2017 Dec;38(6):3419-3429, __2.__ Benjamin P. Levy, 2018 Role of Molecular Profiling in Squamous NSCLC Published Targeted Oncology- Online:Jul 19, 2018, __3.__ (NEW) Hellmann M D et al Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden N Engl J Med 2018; 378:2093-2104, __4.__ Keytruda Prescribing Information . Available at __http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125514s012lbl.pdf__, __5.__ (NEW) Román, M., Baraibar, I., López, I., Nadal,E., Rolfo, C., Vicent, S., & Gil-Bazo, I. (2018). KRAS oncogene in non-small cell lung cancer: clinical perspectives on the treatment of an old target. Molecular Cancer, 17, 33. http://doi.org/10.1186/s12943-018-0789-x , __6.__ Skoulidis, F. et al. STK11/LKB1 co-mutations to predict for de novo resistance to PD-1/PD-L1 axis blockade in KRAS-mutant lung adenocarcinoma [abstract]. J. Clin. Oncol. 35, Suppl., 9016 (2017), __7.__ Ferrara et al Clinical and Translational Implications of RETRearrangements in Non–Small Cell Lung Cancer Journal of Thoracic Oncology 2017 Vol. 13 No. 1, __8.__ News Release FDA. FDA Approves Crizotinib Capsules. (2017). Available from: __http://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm490391.html__, __9.__ (NEW) Finzel A et al The combined analysis of solid and liquid biopsies provides additional clinical information to improve patient care J Cancer Metastasis Treat 2018;4:21., __10.__ (NEW) Laes et al 2018 The clinical impact of using complex molecular profiling strategies in routine oncology practice Oncotarget, 2018, Vol. 9, (No. 29), pp: 20282-20293,

__11.__ For patients with metastatic NSCLC: (1) As single agent in first line if PD-L1 expression tumor proportion score (TPS≥50%) and EGFR / ALK wild type. (2) As single agent after progression under platinum-therapy if PD-L1 expression tumor proportion score (TPS) is above a threshold determined by the FDA for each specific drug therapy regimen., __12__. Overall, TMB has been shown to be a predictive biomarker for immunotherapy. High, intermediate, and low TMB were defined as ≥20 mut/Mb, ≥6 and <20 mut/Mb, or <6 mut/Mb, respectively. It has been reported that a minimum of 1.1 Mb of coding genome can accurately assess this TMB compared with sequencing of the whole exome., __13.__ Mutations in JAK1, JAK2, POLE, STK11, PD-L1, higher number of CNVs, Met-ex14 have been associated with resistance to immunotherapy., __14.__ FDA News Release- FDA approves first cancer treatment for any solid tumor with a specific genetic feature, May 23, 2017 __www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm560167.htm__ accessed on 12 12 2018.

1 Rue Louis Breguet
B-6041 Gosselies, Belgium
+32 (0)71 18 35 00
sales@oncodna.com
www.oncodna.com