OncoDNA®
THE CANCER THERANOSTIC COMPANY

OncoSTRAT&GO
by OncoDNA

OncoSTRAT&GO

THE ONLY MOLECULAR PROFILING SOLUTION COMBINING LIQUID AND SOLID BIOPSIES

Recommended for the following metastatic solid tumours in adults:

HR+, HER2+ AND TRIPLE-NEGATIVE BREAST CANCER • COLORECTAL CANCER • NON-SMALL CELL LUNG CANCER • OVARIAN CANCER • PANCREATIC CANCER • PROSTATE CANCER • CANCER OF UNKNOWN PRIMARY (CUP)

SCREENING MORE THAN THE USUAL SUSPECTS

A unique powerful combination for decision-making

CE IVD

Why combining liquid and solid biopsies?

THERE ARE TWO MAIN REASONS WHY THE COMBINATION OF SOLID AND LIQUID BIOSPIES IS MEANINGFUL IN CLINICAL PRACTICE

1. To decipher tumour spatial heterogeneity (presence of different mutations between the primary tumour and the metastases, as well as between the metastases). This is particularly important in stage IV patients with a cancer for which there are targeted therapies available, in order to identify resistant mutations that may not be present in the solid biopsy analysed. These mutations can be detected in the circulating tumour DNA (ctDNA) (isolated from blood) .

2. To identify germline gene alterations leading to a BRCAness phenotype that are very challenging to detect in FFPE samples. These alterations can be identified in an easier way in DNA from PBMCs (peripheral blood mononuclear cells) (isolated from blood).

OncoSTRAT&GO combines the analysis of a solid biopsy sample (from the primary tumour or a metastasis) and the analysis of a liquid biopsy (blood sample).

ctDNA

→ **In 86% of metastatic patients, solid and liquid biopsies provide different information on genetic alterations** (Finzel A. et al., 2018)

RECOMMENDED FOR :

The following stage IV solid tumours in adults:
- Non-small cell lung cancer
- Breast cancer (HR+ and HER2+)
- Colorectal cancer
- Cancer of unknown primary

DNA of PBMCs

→ **Inherited exon deletions/duplications leading to BRCAness phenotype are difficult to detect in FFPE biopsies (DNA degraded)**

RECOMMENDED FOR :

The following stage IV solid tumours in adults:
- Breast cancer (TNBC)
- Ovarian cancer
- Pancreatic cancer
- Prostate cancer

OncoSTRAT&GO, the most complete solution **integrating the analysis of solid and liquid biopsies**

NEXT-GENERATION SEQUENCING

NEW

PANEL OF 313 GENES

ABL1
ACVR1
ACVR1B
ACVR2A
AJUBA
AKT1
AKT2
AKT3
ALB
ALK
AMER1
APC
APEX1
APLNR
APOB
AR
ARAF
ARHGAP35
ARID1A
ARID2
ARID5B
ATF7IP
ATM
ATP11B
ATR
ATRX
ATXN3
AURKA
AXIN1
AXIN2
B2M
BAP1
BCL2
BCL2L1
BCL2L11
BCL9
BCOR
BIRC2
BIRC3
BRAF
BRCA1
BRCA2
BRD7
BTG2
BTK
CARD11
CASP8
CBL
CCND1
CCND2
CCND3
CCNE1
CD44
CD70
CD79B
CDH1
CHD3
CHD8
CDK12
CDK2
CDK4
CDK6
CDKN2A
CDKN2B
CEBPA
CHD4
CHEK2
COL5A1
CREBBP
CSF1R
CSNK2A1
CTNNB1
CTNND1
CUL1
CUL3
CYP2C19
CYP2D6
DACH1
DCUN1D1
DDR2
DICER1
DNMT3A
DPYD
EEF2
EGFR
ELF3
EP300
EPHA2
EPHA3
EPHA5
ERBB2
ERBB3
ERBB4
ERCC2
ESR1
EZH2
FANCA
FANCC
FANCD2
FANCE
FANCF
FANCI
FANCL
FAS
FAT1
FBXW7
FGF3
FGFR1
FGFR2
FGFR3
FGFR4
FLCN
FLT1
FLT3
FLT4
FOXA1
FOXA2
FOXQ1
GAS6-AS1
GATA1
GATA2
GATA3
GATA6
GNA11
GNAG
GNAS
H3F3A
H3F3C
HGF
HIST1H3B
HNF1A
HRAS
IDH1
IDH2
IGF1R
IL6
IL6ST
IL7R
INSR
JAK1
JAK2
JAK3
KDM6A
KDR
KEAP1
KIT
KNSTRN
KRAS
KMT2A
KMT2B
KMT2C
KMT2D
LYN
MAGOH
MAP2K1
MAP2K2
MAP2K4
MAP3K1
MAP3K4
MAPK1
MDM2
MDM4
MECOM
MED12
MEN1
MET
MGA
MLH1
MPL
MRE11A
MSH2
MSH3
MSH6
MTOR
MUC6
MYC
MYCL
MYD88
MYO18A
NCOR1
NF1
NF2
NFE2L2
NKX2-1
NKX2-8
NOTCH1
NOTCH2
NOTCH3
NPM1
NRAS
NSD1
NTRK1
NTRK2
NTRK3
NUP133
NUP93
PALB2
PAX5
PBRM1
PD-1
PDGFRA
PDGFRB
PD-L1
PD-L2
PIK3CA
PIK3CB
PIK3CG
PIK3R1
PIK3R2
PIM1
POLD1
POLE
PPP2R1A
PPP6C
PRKAR1A
PRKCI
PRKDC
PSIP1
PMS2
PTCH1
PTEN
PTMA
PTPDC1
PTPDC1
PTPN11
PTPRC
PTPRD
RAC1
RAD21
RAD50
RAD51
RAD51B
RAD51C
RAD51D
RAF1
RARA
RASA1
RB1
RBM10
RET
RFC1
RHEB
RHOA
RHOB
RICTOR
RNF43
ROS1
RPS6KA3
RPS6KB1
RPTOR
RQCD1
RRAS2
RUNX1
RUNX1T1
RXRA
SCAF4
SETBP1
SETD2
SF1
SF3B1
SIN3A
SLX4
SMAD2
SMAD4
SMARCA1
SMARCA4
SMARCB1
SMC1A
SMC3
SMO
SOS1
SOX17
SOX2
SOX9
SPOP
SPTA1
SPTAN1
SRC
SRSF2
STAG2
STAT3
STK11
TAF1
TBL1XR1
TBX3
TCEB1
TCF12
TCF7L2
TET2
TGFBR2
TGIF1
THRAP3
TLR4
TMSB4X
TNFAIP3
TOP1
TOP2A
TP53
TPMT
TRAF3
TSC1
TSC2
TSHR
TXNIP
U2AF1
UGT1A1
UNCX
USP9X
VHL
WHSC1
WT1
XPO1
ZFHX3

Solid biopsy

FOR NON-SMALL CELL LUNG, BREAST (HR+, HER2+ AND TRIPLE-NEGATIVE), COLORECTAL, OVARIAN, PANCREATIC AND PROSTATE CANCERS, AND CANCER OF UNKNOWN PRIMARY:

NGS:

313-gene panel for predicting patient response to:

- → Targeted therapies (i.e. PARP inhibitors, EGFR-TKIs, hormonal therapy)
- → Immunotherapy

It includes **LOH**, **TMB** and **MSI** determination, important for immunotherapy response prediction.

Immunohistochemistry (IHC):

Protein expression analysis for predicting patient response to chemotherapies, immunotherapy and targeted therapies.

Additional tests:

Unusual splicing, gene fusions and promoter methylation for predicting patient response to targeted therapies.

NEW

KEY CHANGES IN THE NEW SOLID BIOPSY ANALYSIS

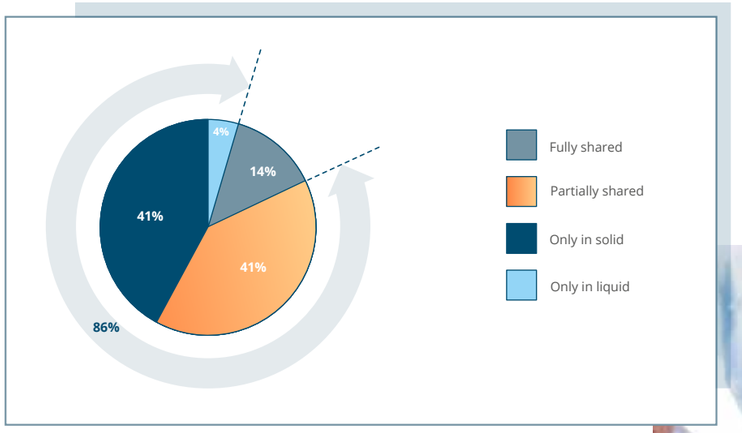
- → **Twice as many genes sequenced (vs previous version)**
  313 instead of 150 genes, leading to a more precise TMB calculation
- → **Microsatellite instability (MSI)**
  Broad coverage beyond the usual markers
- → **Loss of heterozygosity (LOH)**
  More SNP regions covered for determining LOH with a higher accuracy
- → **Fusion panel**
  Detection of fusion events involving ALK, ROS1, RET, FGFR1/2/3 or NTRK1/2/3

1. THE ADDED VALUE OF ctDNA (circulating tumour DNA): Deciphering tumour spatial heterogeneity

ctDNA profiling should be added to the analysis of solid biopsies in clinical routine for metastatic cancer types with targeted therapies available, in order to provide the most comprehensive characterization of the heterogeneity of the patient's tumour (Finzel A. et al., 2018).

IN 86% OF THE PATIENTS, SOLID AND LIQUID BIOPSIES PROVIDE DIFFERENT INFORMATION ON GENETIC ALTERATIONS

Retrospective study evaluating 351 patients with stage IV solid tumours whose tissue and blood samples were tested using the OncoSTRAT&GO profiling solution and who had failed at least one line of therapy before undergoing molecular profiling (Finzel A. et al., 2018).



Patient distribution according to discrepancy between solid and liquid biopsies.
Fully shared: Patients with the same variants detected in solid and liquid biopsies
Partially shared: Patients with variants detected only in the solid or only in the liquid biopsy and with variants detected in both biopsies
Only in solid: Patients with variants detected only in the solid biopsy
Only in liquid: Patients with variants detected only in the liquid biopsy

Liquid biopsy

WHY TO ADD ctDNA PROFILING TO SOLID BIOSPY ANALYSIS?

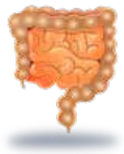
→ To decipher the heterogeneity between the primary tumour and its related metastases, as well as between the different metastatic sites

→ To identifiy drug-resistance mutations that would be responsible of patient's relapse

ONCOSTRAT&GO (SOLID/ctDNA) IS THE ONLY SOLUTION COMBINING LIQUID AND SOLID BIOPSIES AND RECOMMENDED FOR THE FOLLOWING STAGE IV CANCERS:

Non-small cell lung cancer

HR+ and HER+ breast cancer



Colorectal cancer

Cancer of unknown primary

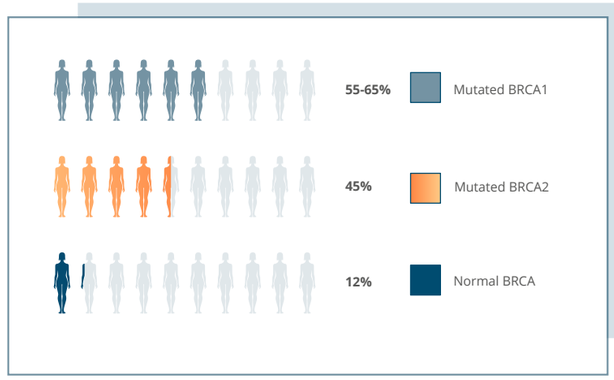
ANALYSIS OF ctDNA

40-gene panel for predicting patient response to immunotherapy and targeted therapies.

AKT1	CKIT	ERRB2	FGFR2	GNAS	JAK3	MTOR	PTEN
ALK	CMET	ESR1	FGFR3	HRAS	KRAS	NPM1	RAF1
AR	CTNNB1	EZH2	FOXL2	IDH1	MAP2K1	NRAS	RET
BRAF	DDR2	FBXW7	GNA11	IDH2	MAP2K2	PDGFRA	ROS1
BTK	EGFR	FGFR1	GNAQ	JAK2	MPL	PIK3CA	TP53

2. THE ADDED VALUE OF DNA FROM PBMCs (peripheral blood mononuclear cells): Identification of germline gene alterations leading to a BRCAness phenotype

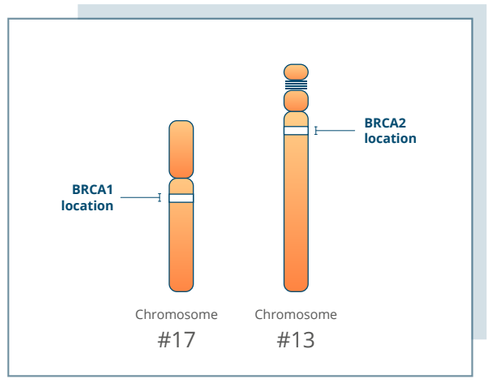
BRCA MUTATIONAL STATUS AND CANCER DEVELOPMENT



Chances of developing breast cancer by age 70.
(Modified from https://www.cancer.gov/research/progress/discovery/brca-cancer-risk-infographic)

Germline mutations in BRCA1 and BRCA2 have been proven to portend an increased lifetime risk of breast, ovarian, prostate and pancreatic cancers in the individuals who carry them.

Of note, about 12% of women in the general population will develop breast cancer sometime during their lives, while about 55-65% of women who inherit a harmful BRCA1 mutation and about 45% of women who inherit a harmful BRCA2 mutation will develop breast cancer by the age of 70.



Location of BRCA1 & BRCA2

BRCA MUTATIONAL STATUS AND RESPONSE TO PARP INHIBITORS

Tumours with mutations in BRCA1/2 or in other genes that when altered lead to homologous recombination deficiency (BRCAness phenotype) are particularly sensitive to PARP inhibitors.

In fact, PARP inhibitors have been approved by the FDA for the treatment of breast and ovarian cancers with germline mutations in the BRCA1 or BRCA2 gene.

LIMITATION OF FFPE SAMPLES

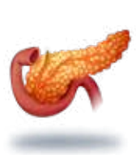
About 5-10% of BRCA1/2 mutations are exon deletions/duplications, very difficult to detect in FFPE samples. As these alterations are germline, they can be identified in normal DNA from PMBCs.

WHY TO ADD PROFILING OF DNA FROM PMBCs TO SOLID BIOPSY ANALYSIS?

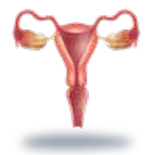
→ To identify patients sensitive to PARP inhibitors harboring BRCA1/2 alterations difficult to detect in FFPE samples (or in ctDNA)

ONCOSTRAT&GO (SOLID/PBMCs DNA) IS THE ONLY SOLUTION COMBINING LIQUID AND SOLID BIOPSIES AND RECOMMENDED FOR THE FOLLOWING STAGE IV CANCERS:

Triple-negative breast cancer



Pancreatic cancer



Ovarian cancer

Prostate cancer

ANALYSIS OF DNA FROM PBMCs

Panel for detecting germline exon deletions/duplications, which are very challenging to detect in solid biopsies (as well as in ctDNA). In addition to BRCA1/2, we also test other genes involved in the BRCAness phenotype:

APC	BRCA1	CDKN2A	MLH1	MSH6	PALB2	POLE	RAD51D
ATM	BRCA2	CHEK2	MRE11A	MUTYH	PIK3CA	PTEN	SCG5 (dup only)
BAP1	BRIP1	EPCAM	MSH2	NBN	PMS2	RAD50	SMAD4
BARD1	CDH1	GREM1	MSH3	NTHL1	POLD1	RAD51C	STK11

NEW

KEY CHANGES IN THE NEW LIQUID BIOPSY ANALYSIS

→ **New BRCAness panel**

To determine response to PARP inhibitors in a broader population of patients

→ **Adapted technology**

From normal DNA extracted from blood samples, using a technology that enables the detection of exon deletions/duplications with high accuracy

About 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 tumour 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 tumour 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 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 tumours (stage III or IV) in adults
- Glioblastoma in children

SOLID AND LIQUID BIOPSIES:

OncoSTRAT&GO

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 tumour DNA (for deciphering tumour 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 tumour, 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 tumours in adults:

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

NO SOLID BIOPSY:

OncoSELECT®

CANCER-SPECIFIC SOLUTION FROM A LIQUID BIOPSY SAMPLE

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

It is the perfect solution to identify therapeutic options for cancer patients not able to have their tumour 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 stage IV solid tumours in adults:

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

MONITORING RESPONSE:

OncoDNA can also provide a solution for personalised monitoring.

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

OncoSTRAT&GO results in an integrated theranostic report

1 MEDICAL INFORMATION

- High definition image of the tumour sample
- Clinical form with patient clinical data
- Cancer type and stage

2 NEXT-GENERATION SEQUENCING

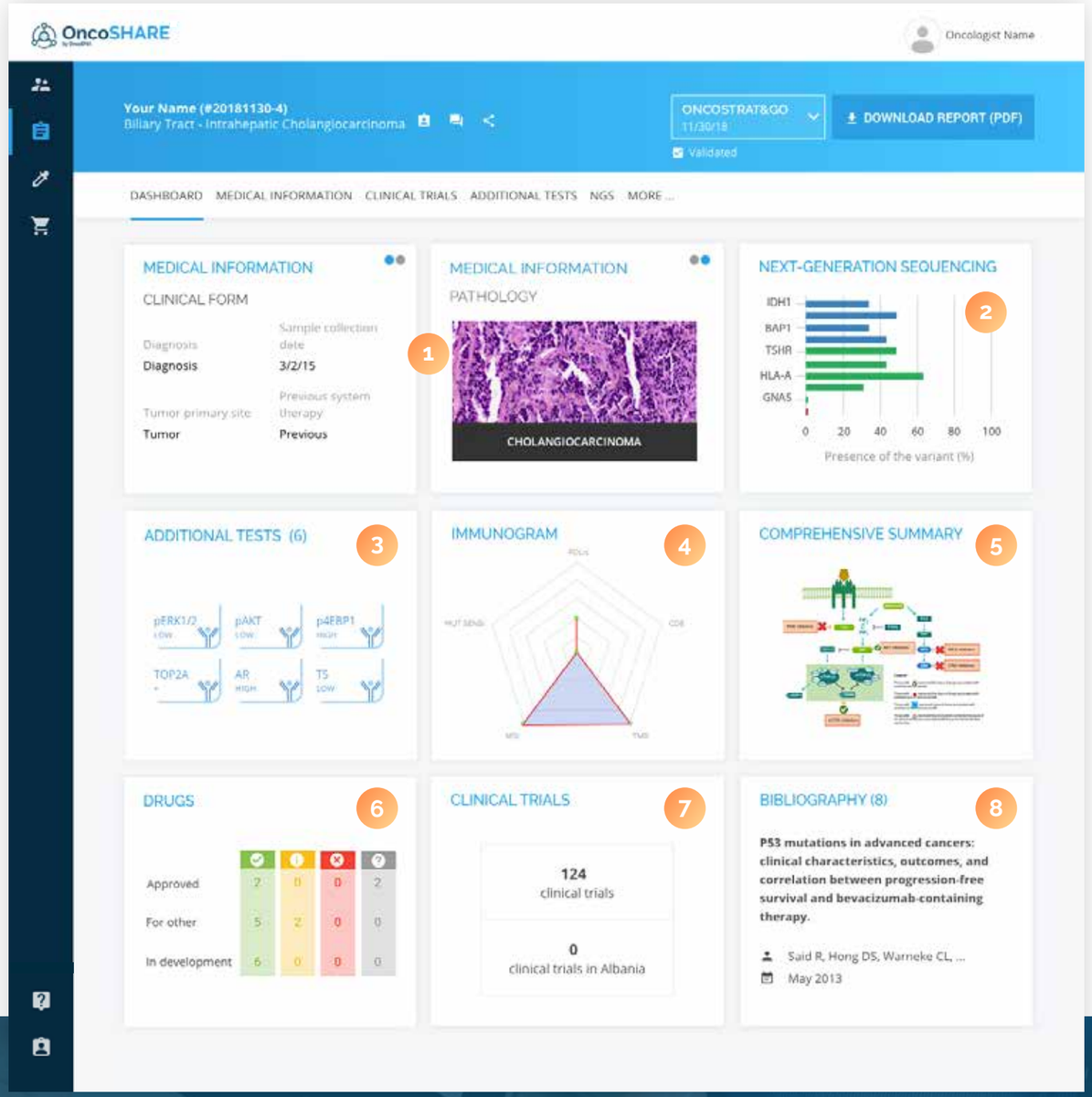
- Complete list of variants and their biological and therapeutical impact
- List of genes sequenced
- MSI (microsatellite instability)
- TMB (tumour mutational burden)
- Alpha list: Biomarkers associated with FDA and/or EMA approved drugs with pharmacogenomic information on their labels, as well as variants associated with clinical resistance or sensitivity to FDA/EMA approved drugs

3 ADDITIONAL TESTS

- Immunohistochemistry (for chemotherapy, targeted therapy or immunotherapy response prediction)
- Unusual splicing and methylation
- Translocations or fusions

4 IMMUNOGRAM

The immunogram shows the potential response of each patient to immunotherapy. It is created from (1) the percentage of PD-L1-positive tumour cells, (2) the percentage of infiltrated CD8+ T cells, (3) the level of tumour mutational burden, (4) the microsatellite stability status of the tumour, and (5) the presence of mutations associated with either sensitivity or resistance to immunotherapy.
The larger the area, the better the patient should respond to immunotherapy.



5 COMPREHENSIVE SUMMARY

- List of treatments that could be associated with clinical benefit, as well as those that may not provide any benefit
- Simplified molecular pathway(s)

6 DRUGS

- List of treatments associated with:
  - Potential clinical benefit
  - Potential lack of clinical benefit
  - Undetermined clinical benefit
  - Toxicity
- Trade names, therapeutic classes, official indications
- Approval status for the type of cancer and for other indications
- Drugs in development

7 CLINICAL TRIALS

List of all clinical trials associated with certain features of the molecular profile of the patient.

8 BIBLIOGRAPHY

List of all publications used in the report that are related to the patient's molecular profile.

How to order an OncoSTRAT&GO test?

1 LOGIN TO OncoSHARE by OncoDNA

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

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

Regardless of whether we are dealing with information about patient health or payment, we take every precaution to ensure your security. OncoSHARE is used by oncologists to order our solutions, to display interactive analysis reports and to 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 tumour.

www.oncoshare.com

2 ORDERING THE ONCOSTRAT&GO SOLUTION

2.1. Proceed to payment (credit card or wire transfer)
2.2. We ship the corresponding sample collection kit to you

3 COLLECT THE SAMPLE

Collect the biopsy and send the kit back to OncoDNA. Please print your own prepaid shipping label generated online at https://delivery.oncodna.com.

4 SAMPLE ANALYSIS

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

5 YOUR REPORT READY ON ONCOSHARE

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

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).**

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SCREENING MORE THAN THE USUAL SUSPECTS

A unique powerful combination for decision-making

REFERENCES :

• ***Finzel A.*** *et al. The combined analysis of solid and liquid biopsies provides additional clinical information to improve patient care. J Cancer Metastasis Treat. 4:21 (2018).*

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