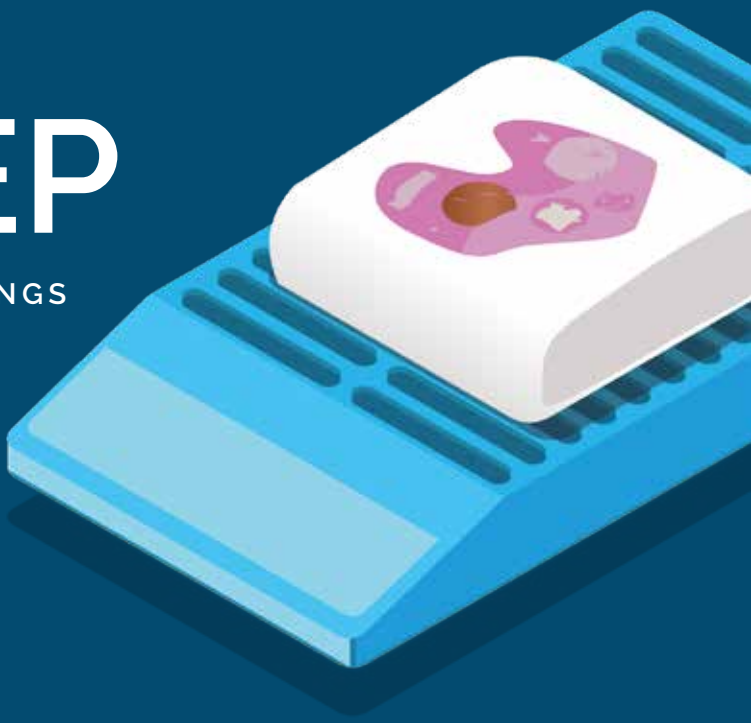
OncoDNA® THE CANCER THERANOSTIC COMPANY | OncoDEEP® by OncoDNA

OncoDEEP

OUR UNIQUE SOLUTION COMBINING NGS AND PROTEIN ANALYSES OF A SOLID TUMOR SAMPLE



SCREENING MORE THAN THE USUAL SUSPECTS

Combination is Key for Clinical Benefit

CE IVD

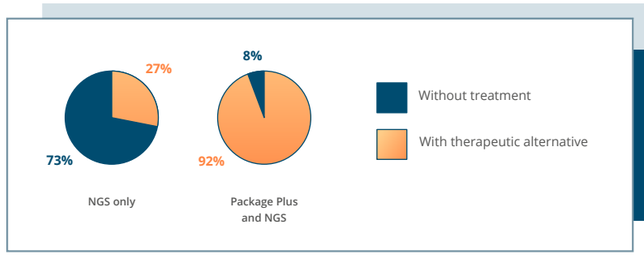
Clinical evidence: Combination of profiling methods is essential

COMBINATION OF DIFFERENT PROFILING METHODS IN ADVANCED CANCER PATIENTS AFTER TREATMENT(S) FAILURE

NEW

1,057 patients in 30 countries (4 continents) were treated by oncologists using OncoDNA's molecular profiling & Information Services

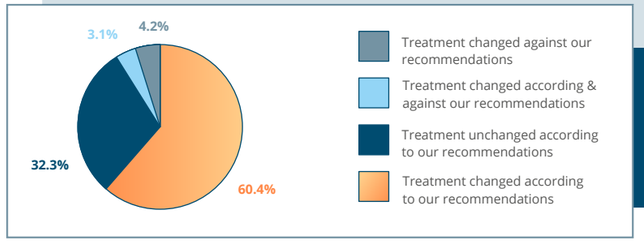
1. NGS alone is not enough to decide for treatment



For 92% of the oncologists, combining NGS with Package Plus* data results has a better clinical insight.

Patients with treatment options (approved for the cancer type analysed, approved for other cancer types or under development) and without, according to test;

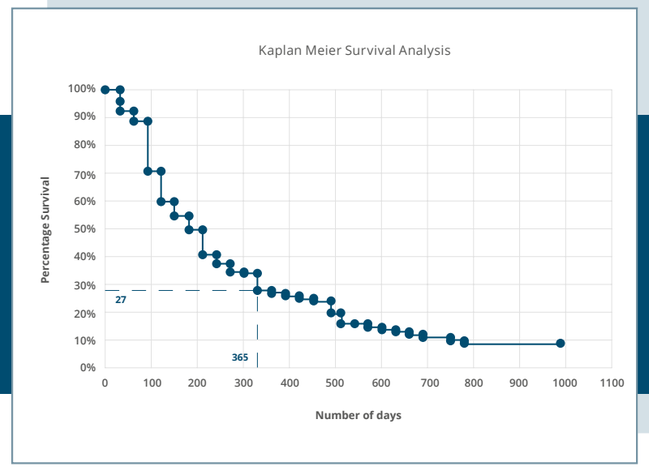
2. Adoption of our holistic approach



92.7% of the oncologists agreed with OncoDNA's recommendations.

Results of oncologist survey. Treatment choices according and against recommendations;

3. Improved overall survival



3. Overall survival of patients. For the cases where our recommendations were followed (n=114), the overall survival was analysed.

Based on OncoDNA approach, at least 50% of the patients had an OS of > 6 months, and 27% of patients had a minimum overall survival > 12 months (expected OS of ~3 - 6 months) (Laes et al 2018)

***Package plus includes additional test of imunohistochemistry (IHC) for chemo, immuno and targeted therapies, and other molecular test like: methylation of the MGMT promoter, the expression of either EGFRVIII, MET protein, receptor tyrosine kinase (MET)- exon 14 deletion or androgen-receptor splice variant 7 (ARV7), and microsatellite instability testing.**

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

> Molecular characterization of the tumor using next generation sequencing (NGS) technology, has become a **key tool** for facilitating treatment decisions and the clinical management...
>
> **Tsoulos et al 2017**

> Diagnostics and gene expression platforms are considered helpful **when used to complement IHC testing**, because the results they are providing can be compared against many databases, allowing more accurate diagnosis...
>
> **F. Losa et al 2018**


The clinical impact of using complex molecular profiling strategies in routine oncology practice

OncoDEEP is the gold standard combination of molecular profilings

THE BEST SET OF DATA FOR IMMUNOTHERAPY SELECTION

Thanks to the best market proposal for combination of druggable DNA/RNA mutations detection, TMB, MSI, LOH (lost of heterozygosity), Fusion Panel, IHC, ...

NEW THE NEW VERSION OF ONCODEEP

4 times more genes & gene regions

313 GENES INSTEAD OF 75

- → Including genes involved in Homologous Recombination Deficiency (HRD) for PARP inhibitors
- → Including more genes involved in immunotherapy selection
- → Strongly enlarged panel of genes for improved TMB and MSI calculation

Microsatellite instability (MSI)

FOR ONCODNA THE USUAL SUSPECTS ARE NOT ENOUGH

- → Broader coverage to increase the accuracy of our algorithm

Unique design for LOH

UNEQUALLED POWER

- → More SNPs for heterozygosity and LOH analysis for key genes associated with response to immunotherapy
- → OncoDEEP is the only product assessing either homozygotous or heterozygotous deletion of genes in relationship with immunotherapy

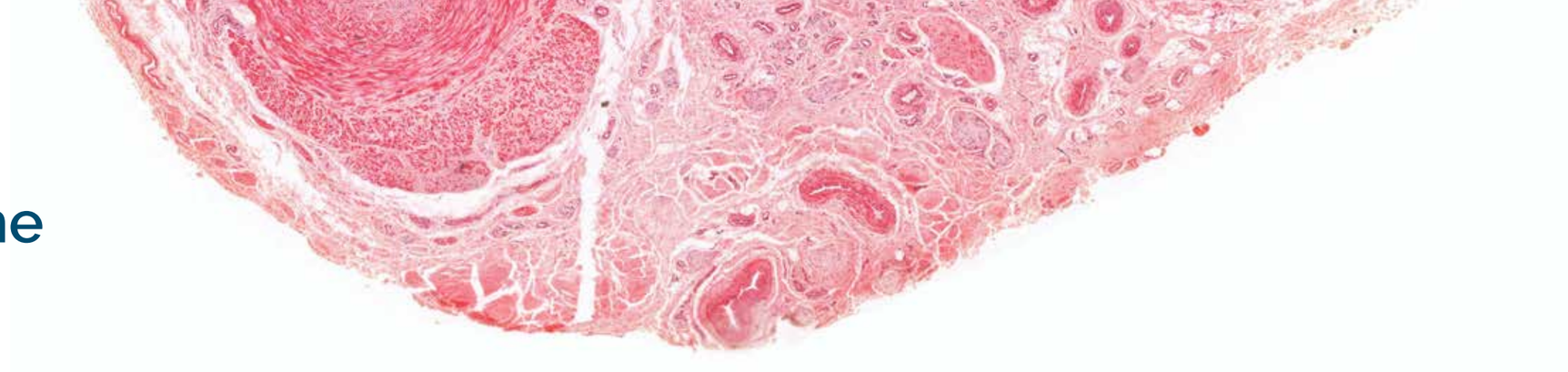
Fusion Panel (RNA Seq)

ON TOP OF CLASSICAL SUSPECTS

OncoDEEP enable detecting broader fusions (even for unknown partner) and a broader detection with new :

- → probes for NTRK1 / 2 and 3
- → probes to detect MET-ex14 and EGFRVIII
- → probes to allow the quantification of the expression of FGFR1 / 2 & 3
- → probes for ALK / ROS1 / RET

OncoDEEP screens the tumors much beyond the usual suspects



NEXT GENERATION SEQUENCING (NGS) - 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
GNAQ
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
MYCN
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
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

XXX : Usual hospitals routine xxx : New in OncoDEEP V6 xxx : Already in previous version

GENES LIST BY THERAPY

Some examples of useful genes for targeted therapies :

AKT1
ALK
AR
ARID1A
BRAF
BRCA1
CCND1
CCNE1
CDK4
CDK6
CDKN2A
CDKN2B
CHEK2
CSF1R
CTNNB1
CYP2C19
CYP2D6
DPYD
EGFR
ERBB2
ERBB3
ERBB4
ESR1
EZH2
FANCA
FANCC
FANCD2
FANCE
FANCF
FANCI
FANCL
FBXW7
FGFR1
FGFR2
FGFR3
FGFR4
GNA11
GNAQ
GNAS
HIST1H3B
HRAS
IDH1
IDH2
IGF1R
JAK2
KIT
KRAS
MAP2K1
MAP2K2
MET
MTOR
NRAS
NTRK1
NTRK2
NTRK3
PALB2
PDGFRA
PDGFRB
PIK3CA
PTEN
RAC1
RAD51
RAD51B
RAD51C
RAD51D
RAF1
RB1
RET
ROS1
SMAD4
SMO
TPMT
TSC1
TSC2
VHL

Some examples of useful genes for immunotherapies :

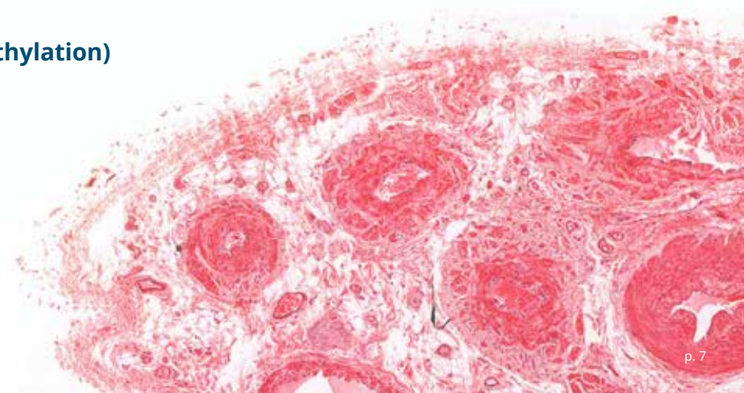
ARID2
APLNR
B2M
BRD7
JAK1
JAK2
JAK3
MLH1
MSH2
MSH6
PBRM1
PD-1
PD-L1
PD-L2
POLD1
POLE
PMS2
PTEN
STK11

Some examples of useful genes for PARP inhibitors :

ARID1A
ATM
BRCA1
BRCA2
CHEK2
FANCA
FANCC
FANCD2
FANCE
FANCF
FANCI
FANCL
FAS
PALB2
RAD51
RAD51B
RAD51C
RAD51D

CANCER TYPE SPECIFIC PACKAGE

- → **IHCs for targeted therapies**
- → **IHCs for chemotherapies**
- → **IHCs for immunotherapies**
- → **Other (translocation analysis, methylation)**
- → **Immunogram (MSI + TMB)**



OncoDEEP Key actionable genes and gene region

- **EGFR-TKI's**
  erlotinib, gefitinib, afatinib, osimertinib, dacomitinib, ...
  EGFR | KRAS | MET | ERBB2

- **RET inhibitors**
  cabozantinib, ...
  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, JAK3, MLH1, MSH2, MSH6, PBRM1, PD-1, POLD1, POLE, PMS2, PTEN, STK11

XXX : Usual hospital routine

: DNA/RNA

: Protein

EXAMPLES OF CLINICAL EVIDENCE BEYOND THE USUAL SUSPECTS

Non-Small Cell Lung Cancer

STK11 inactivation and immunotherapy resistance

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 high likelihood of response. Precision immunotherapy will require tailoring to the co-mutation status of individual tumour (Stoulikis 2017)

Cancer of Unknown Primary

NGS alone is not sufficient for accurate decisions

Molecular diagnostics and gene expression platforms are considered helpful when used to complement IHC testing for tissue of origin assessment allowing more accurate diagnosis and specification of tumour origins recommended as part of the standard evaluation for selected patients with CUP (Consensus doc. SEAP-SEOM, 2018) (F. Losa et al 2018)

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 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 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**

OncoDEEP results in an integrated theranostic report

1 MEDICAL INFORMATION

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

2 NEXT-GENERATION SEQUENCING

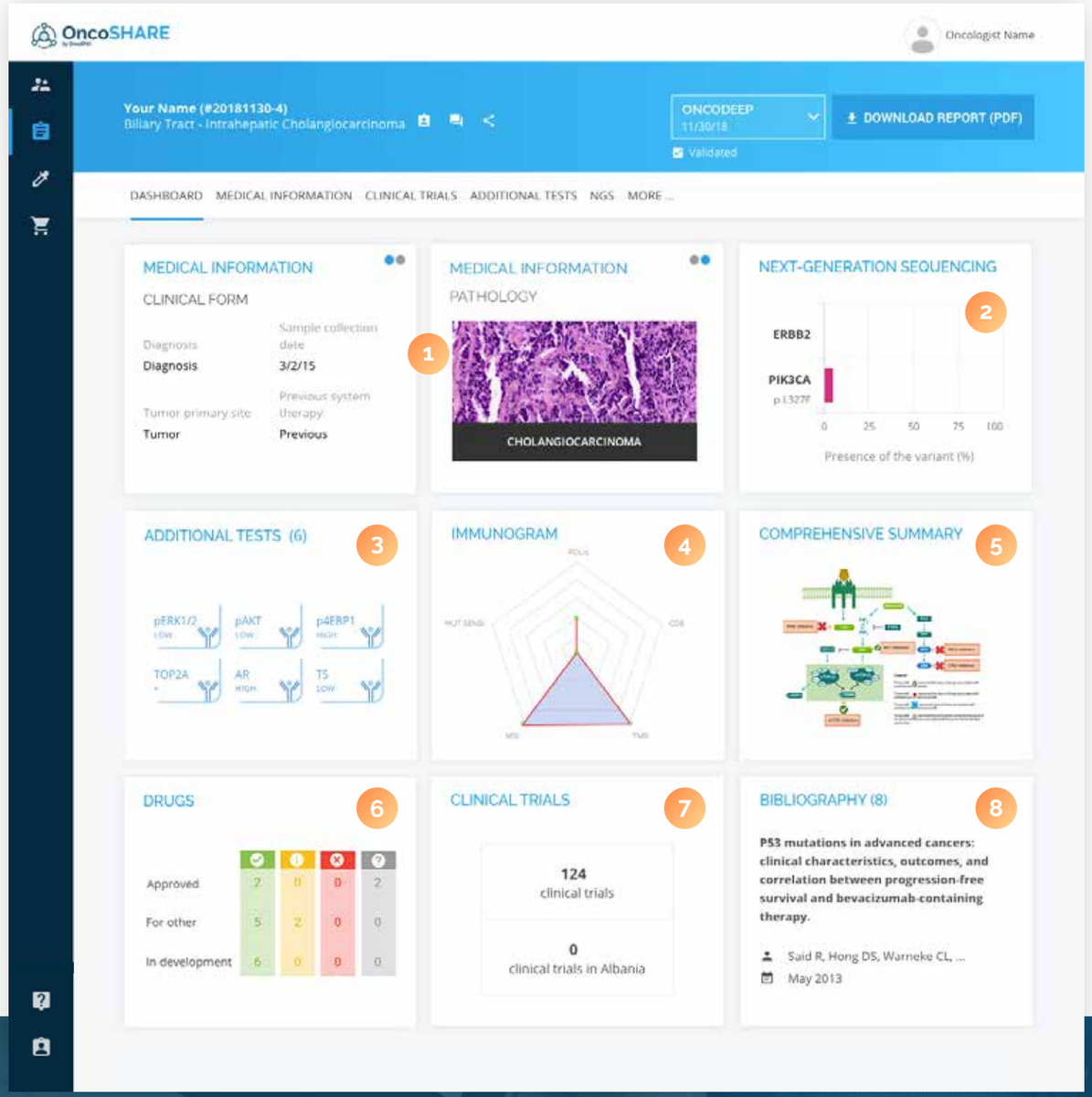
- Complete list of variants and their biological and therapeutical impact
- List of genes sequenced
- MSI (microsatellite instability)
- TMB (tumor mutational burden)
- Alphalist: Biomarkers associated with FDA and/or EMA approved drugs with pharmacogenomic information on their labels as well as variants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

3 ADDITIONAL TESTS

- Immunohistochemistry (for chemotherapy, targeted therapy or immunotherapy)
- 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 tumor cells, (2) the percentage of infiltrated CD8+ T cells, (3) the level of tumor mutational burden, (4) the microsatellite stability status of the tumor (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 should be associated with clinical benefits, as well as those that shouldn't
- Simplified molecular pathway(s)

6 DRUGS

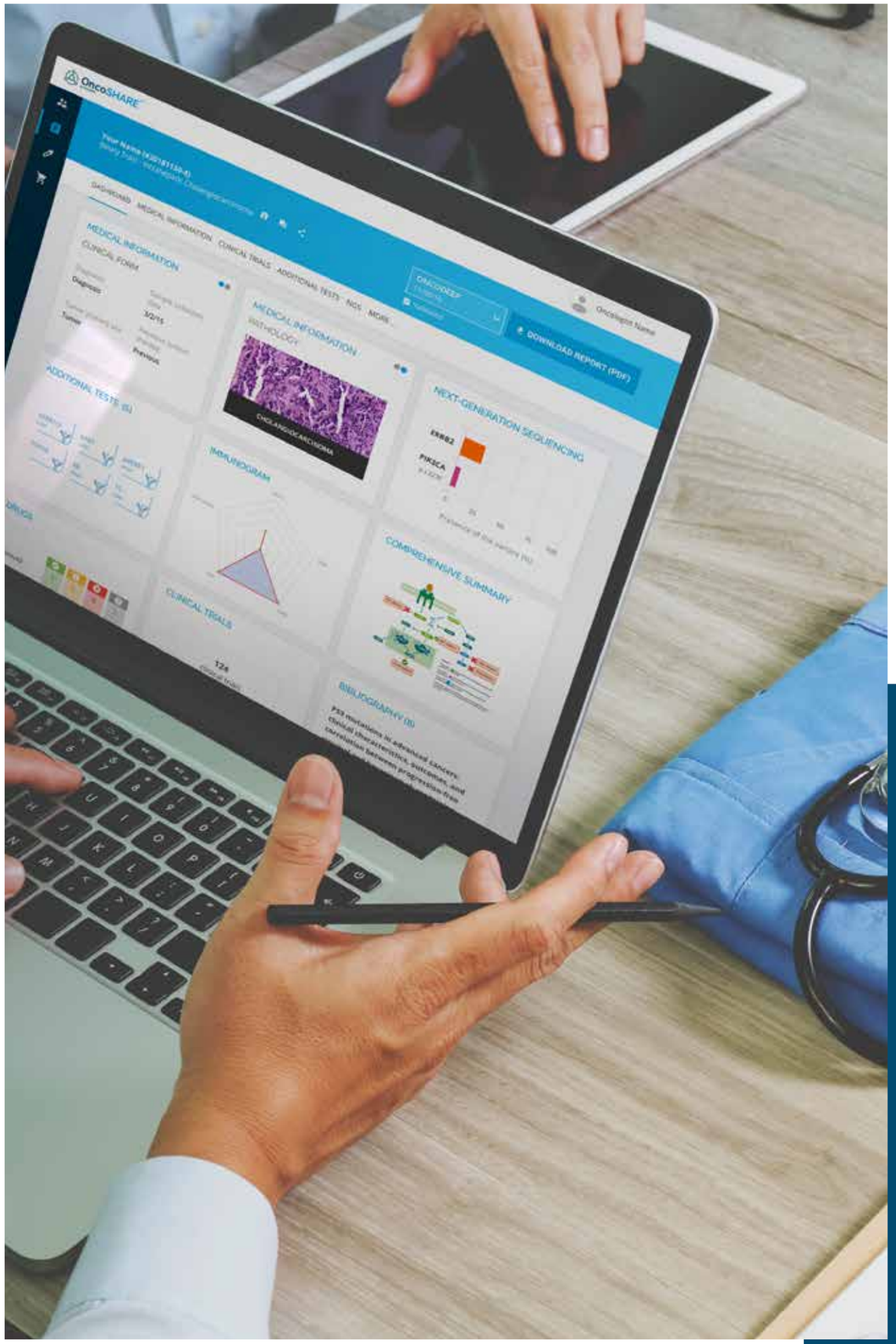
- List of treatments associated with:
  - Potential clinical benefit
  - Potential lack of clinical benefit
  - Undetermined clinical benefit
  - Toxicity
- Tradenames, therapeutic classes, official indications
- Approval status for the type of cancer and for other indications
- Drugs in development

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 and links related to the patient's molecular profile used in the report.



How to order an OncoDEEP 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 information concerns 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 tumor.

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 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 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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Combination is Key for Clinical Benefit

REFERENCES :

__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) __Toulos__ N 20017 Oncol Rep. 2017 Dec;38(6):3419-3429. doi: 10.3892/or.2017.6051. Epub 2017 Oct 23. __Losa__ et al 2018 Clin Transl Oncol. 2018 May 28. doi: 10.1007/s12094-018-1899-z __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

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