



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

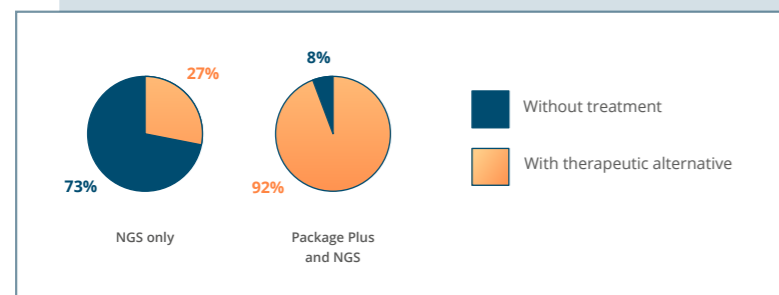


Clinical evidence: Combination of profiling methods is essential

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

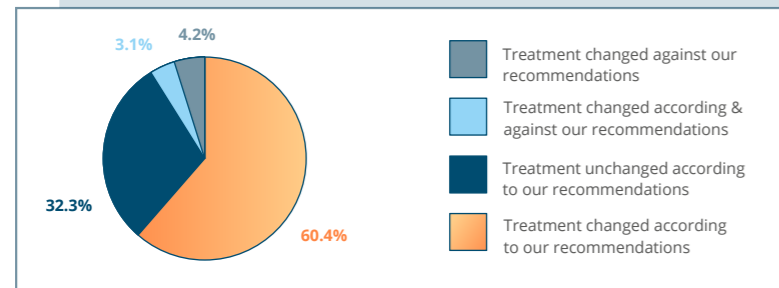
NEW 1,057 patients in 30 countries (4 continents) were treated by oncologists using OncoDNA's molecular profiling & Information Services

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.

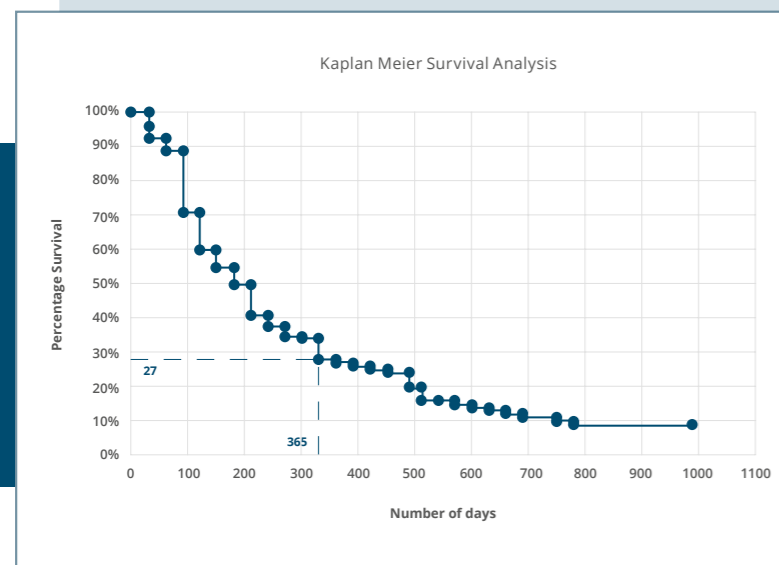
2. Adoption of our holistic approach



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

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

3. Improved overall survival



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

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

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 immunohistochemistry (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



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

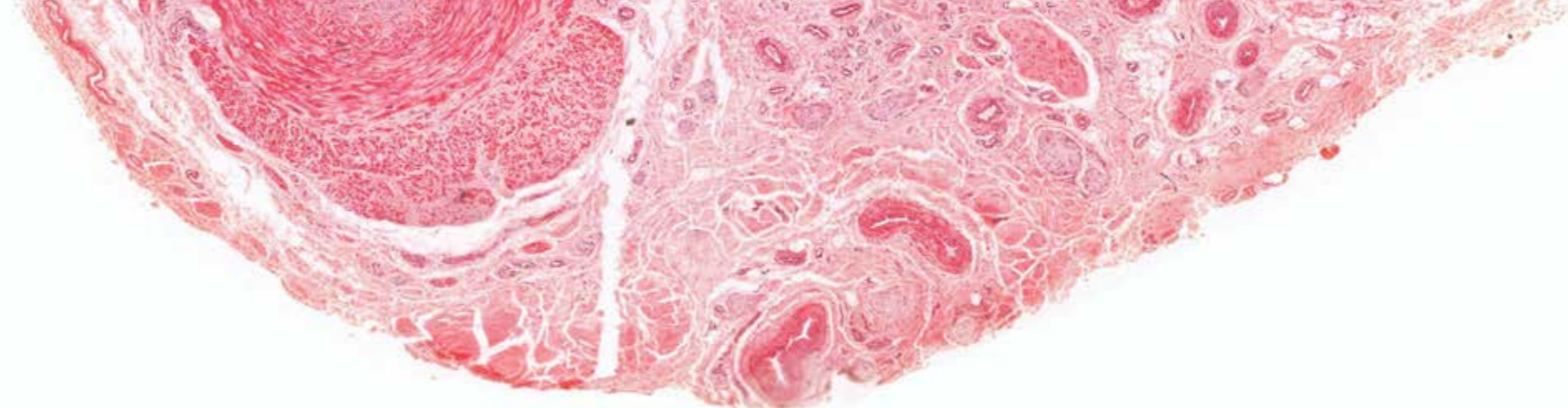
- More SNPs for heterozygosity and LOH analysis for key genes associated with response to immunotherapy
- OncoDEEP is the only product assessing either homozygous or heterozygous deletion of genes in relationship with immunotherapy

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	BCL9	CSNK2A1	FBXW7	JAK2	MYC	PIM1	RNF43	STAT3
ACVR1	BCOR	CTNNB1	FGF3	JAK3	MYCL	POLD1	ROS1	STK11
ACVR1B	BIRC2	CTNND1	FGFR1	KDM6A	MYCN	POLE	RPS6KA3	TAF1
ACVR2A	BIRC3	CUL1	FGFR2	KDR	MYD88	PPP2R1A	RPS6KB1	TBL1XR1
AJUBA	BRAF	CUL3	FGFR3	KEAP1	MYO18A	PPP6C	RPTOR	TBX3
AKT1	BRCA1	CYP2C19	FGFR4	KIT	NCOR1	PRKAR1A	RQCD1	TCEB1
AKT2	BRCA2	CYP2D6	FLCN	KNSTRN	NF1	PRKCI	RRAS2	TCF12
AKT3	BRD7	DACH1	FLT1	KRAS	NF2	PRKDC	RUNX1	TCF7L2
ALB	BTG2	DCUN1D1	FLT3	KMT2A	NFE2L2	PSIP1	RUNX1T1	TET2
ALK	BTK	DDR2	FLT4	KMT2B	NKX2-1	PMS2	RXRA	TGFB2
AMER1	CARD11	DICER1	FOXA1	KMT2C	NKX2-8	PTCH1	SCAF4	TGIF1
APC	CASP8	DNMT3A	FOXA2	KMT2D	NOTCH1	PTEN	SETBP1	THRAP3
APEX1	CBL	DPYD	FOXQ1	LYN	NOTCH2	PTMA	SETD2	TLR4
APLN	CCND1	EEF2	GAS6-AS1	MAGOH	NOTCH3	PTPDC1	SF1	TMSB4X
APOB	CCND2	EGFR	GATA1	MAP2K1	NPM1	PTPN11	SF3B1	TNFAIP3
AR	CCND3	ELF3	GATA2	MAP2K2	NRAS	PTPRC	SIN3A	TOP1
ARAF	CCNE1	EP300	GATA3	MAP2K4	NSD1	PTPRD	SLX4	TOP2A
ARHGAP35	CD44	EPHA2	GATA6	MAP3K1	NTRK1	RAC1	SMAD2	TP53
ARID1A	CD70	EPHA3	GNA11	MAP3K4	NTRK2	RAD21	SMAD4	TPMT
ARID2	CD79B	EPHA5	GNAQ	MAPK1	NTRK3	RAD50	SMARCA1	TRAF3
ARID5B	CDH1	ERBB2	GNAS	MDM2	NUP133	RAD51	SMARCA4	TSC1
ATF7IP	CHD3	ERBB3	H3F3A	MDM4	NUP93	RAD51B	SMARCB1	TSC2
ATM	CHD8	ERBB4	H3F3C	MECOM	PALB2	RAD51C	SMC1A	TSHR
ATP11B	CDK12	ERCC2	HGF	MED12	PAX5	RAD51D	SMC3	TXNIP
ATR	CDK2	ESR1	HIST1H3B	MEN1	PBRM1	RAF1	SMO	U2AF1
ATRX	CDK4	EZH2	HNF1A	MET	PD-1	RARA	SOS1	UGT1A1
ATXN3	CDK6	FANCA	HRAS	MGA	PDGFRA	RASA1	SOX17	UNCX
AURKA	CDKN2A	FANCC	IDH1	MLH1	PDGFRB	RB1	SOX2	USP9X
AXIN1	CDKN2B	FANCD2	IDH2	MPL	PD-L1	RBM10	SOX9	VHL
AXIN2	CEBPA	FANCE	IGF1R	MRE11A	PD-L2	RET	SPOP	WHSC1
B2M	CHD4	FANCF	IL6	MSH2	PIK3CA	RFC1	SPTA1	WT1
BAP1	CHEK2	FANCI	IL6ST	MSH3	PIK3CB	RHEB	SPTAN1	XPO1
BCL2	COL5A1	FANCL	IL7R	MSH6	PIK3CG	RHOA	SRC	ZFH3
BCL2L1	CREBBP	FAS	INSR	MTOR	PIK3R1	RHOB	SRSF2	
BCL2L11	CSF1R	FAT1	JAK1	MUC6	PIK3R2	RICTOR	STAG2	

GENES LIST BY THERAPY

Some examples of useful genes for targeted therapies :

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

Some examples of useful genes for immunotherapies :

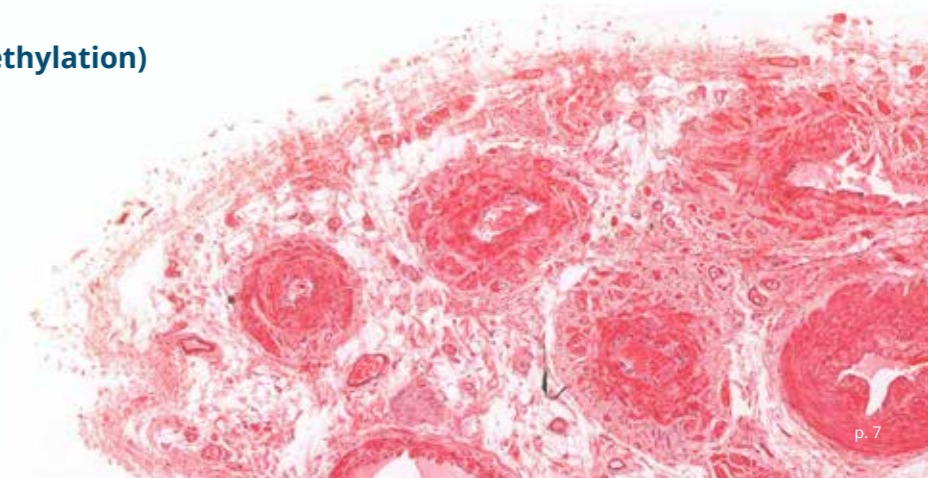
ARID2	JAK2	PBRM1	POLE
APLN	JAK3	PD-1	PMS2
B2M	MLH1	PD-L1	PTEN
BRD7	MSH2	PD-L2	STK11
JAK1	MSH6	POLD1	

Some examples of useful genes for PARP inhibitors :

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











CANCER TYPE SPECIFIC PACKAGE

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



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

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 hospitals 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.

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

SOLID BIOPSY:



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 the 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:



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:



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 provide also a solution for personalized monitoring.

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

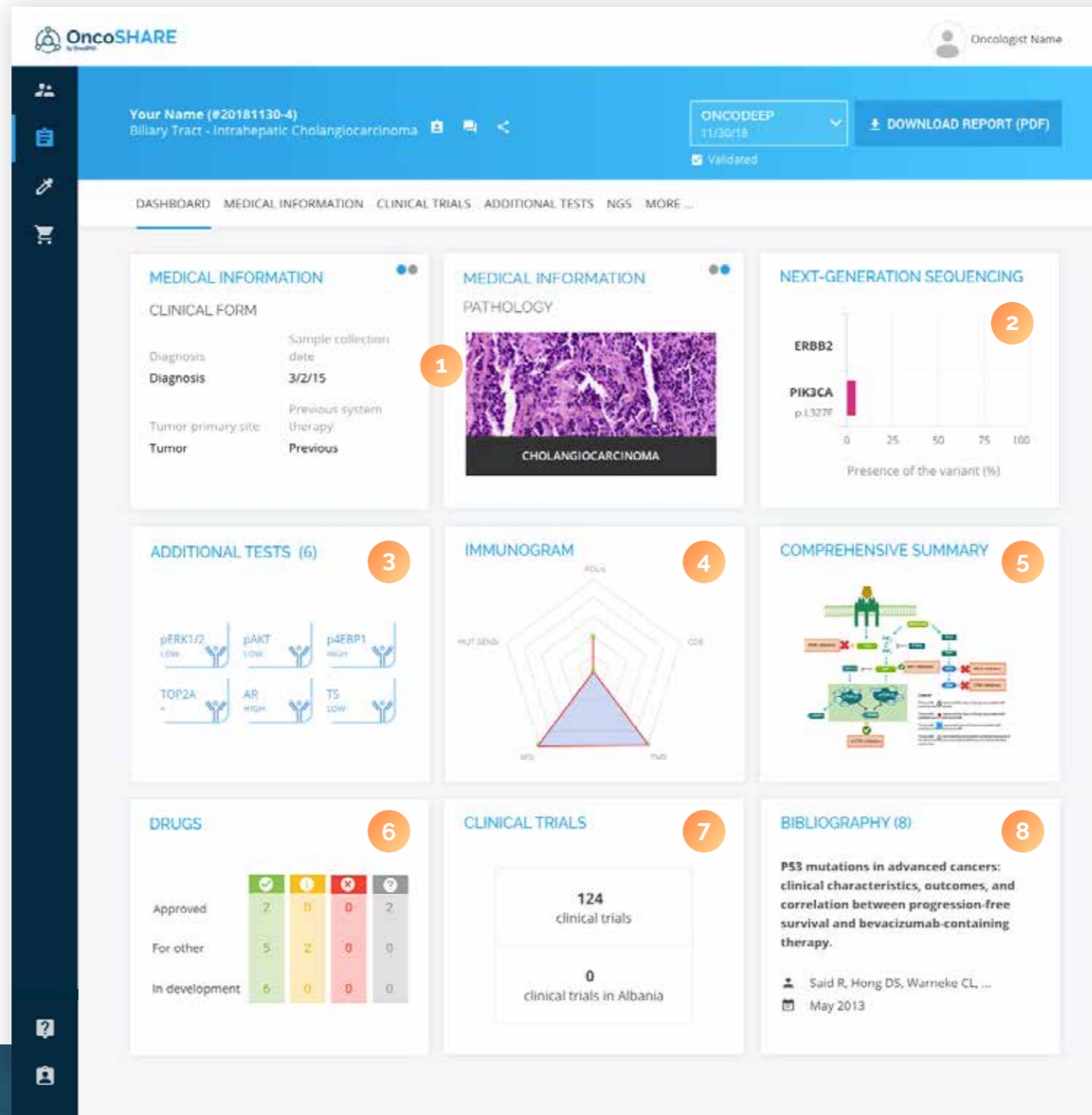
3 ADDITIONAL TESTS

- 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 treatment classes associated with clinical benefit or not
- 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 ONCODEEP SOLUTION

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

3 COLLECT THE SAMPLE

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

4 SAMPLE ANALYSIS

On arrival at the OncoDNA facilities, the sample quality is checked and the sample 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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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