Fully automated end-to-end IVD solution for ultra fast NGS results? *Yes, we can*

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Disclaimer

This presentation is intended for **educational purposes**, the information and data displayed do not replace independent professional judgment.
Besides the ***Ion PGM Dx System***, ***Ion Torrent Genexus Dx system****, the ***Oncomine Dx Target Test*** and ***Oncomine Dx Express Test,*** none of the Oncomine Assays is currently approved for clinical or diagnostic use.

*European CE-IVD certification

Agenda Overview

1 **Precision Medicine: the Impact of Genomic Profiling**
Molecular testing and patient survival

2 **Introducing the Oncomine Dx Express Test**
The daily oncology biomarker profiling assay for any lab

3 **ODx ET External Site Evaluation Study**
Highlighting ODx ET capability and reproducibility across sites

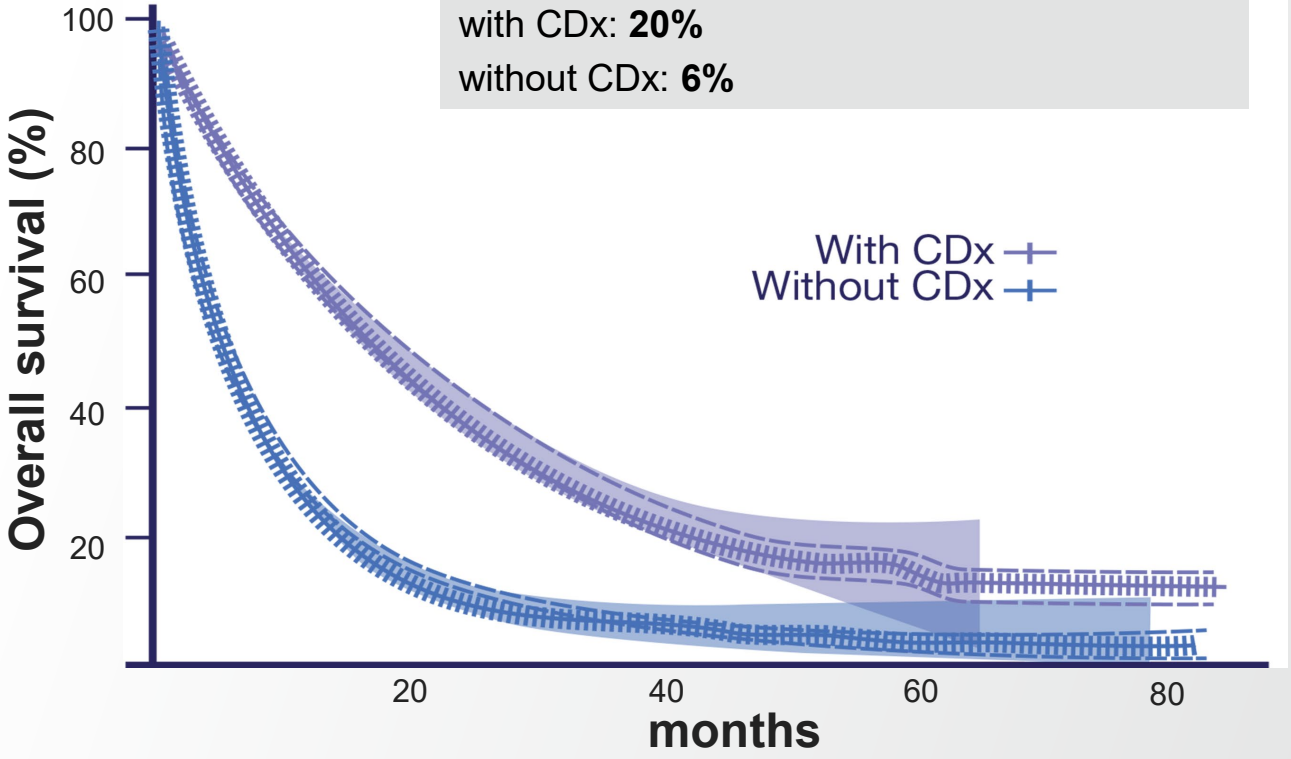
Precision oncology helps improve patient outcomes

Non-small cell lung cancer (NSCLC) patients who received biomarker-driven therapy as first line have better survival rates

% Overall Survival at 60 months

with CDx: **20%**

without CDx: **6%**



Timely patient access to testing is a critical first step to inform individualized treatment strategies

CDx = companion diagnostics

Adapted from John A et al. (2020) *Oncologist* 25:e1743

Genomic profiling-directed therapy improves patient outcomes

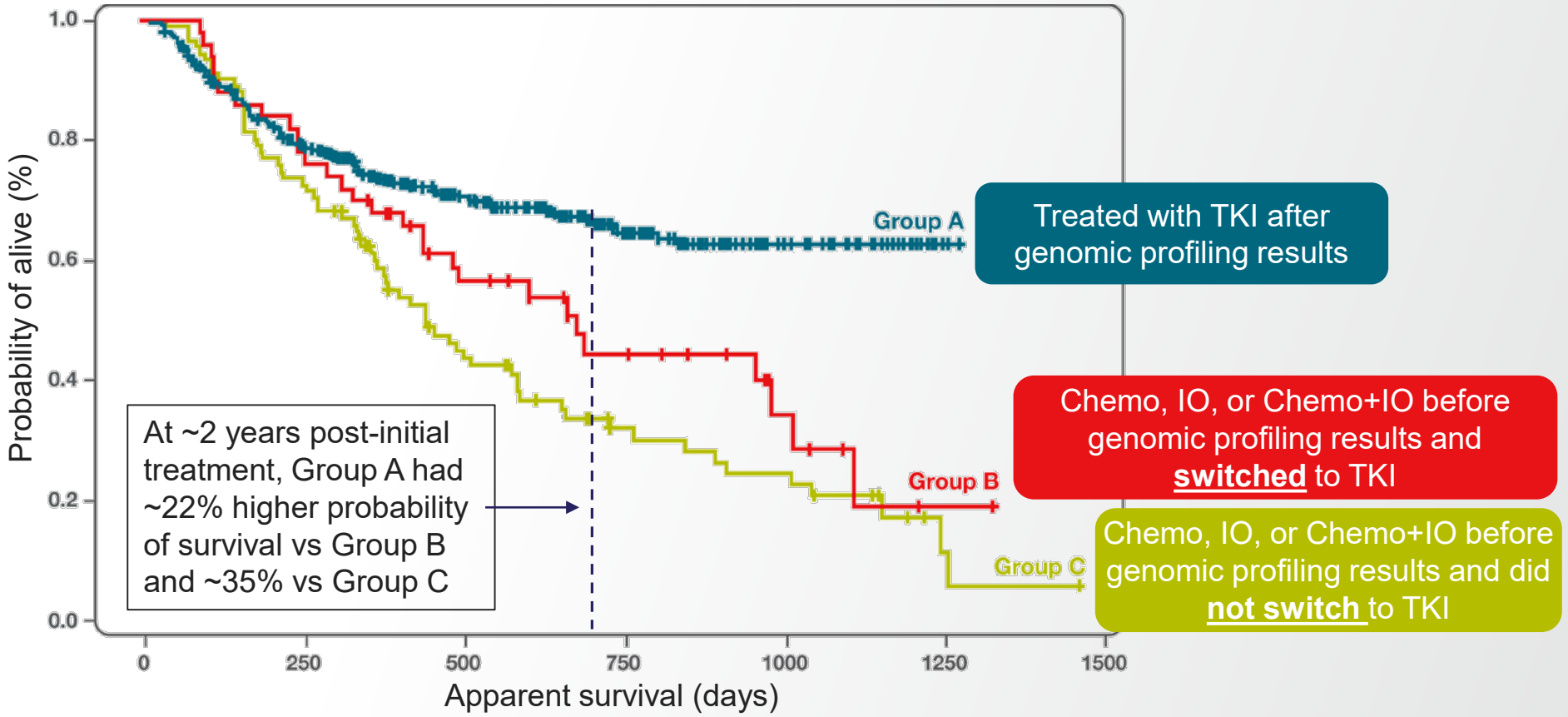
Retrospective study of **525** newly diagnosed stage IV NSCLC patients harboring actionable oncogenic drivers[1,2]

24.7 days

Average turnaround time of NGS-based tumor biomarker results in U.S.

27.3%

Cancer patients are treated *before* molecular profiling results are delivered.



Patients treated based on molecular test results have better clinical outcomes – but results are needed faster, closer to the patient.

1. Smith RE, et al., J Clin Oncol 40, 2022 suppl 16; abstr 15300; 2. Choksi et al., ESMO 2022

IonTorrent solutions success rate – No one is like us

	STRATA ONCOLOGY (US) (1) (Samples collected from 39 US Medical Centers[1])	*HEIDELBERG HOSPITAL (DE)* (2)	*LC-SCRUM (JP)* (3)	*UNIVERSITE' COTE D'AZUR (FRA)* (4)
		GeneStutio/S5		Genexus System
# samples	*(all cancers)* **32,048**	*(lung cancer)* **3,109**	*(lung cancer)* **10,667**	*(lung cancer)* **259**
Test Success Rate	**94.2%**	**96.6%**	**94.5%**	**96.0%**
Turnaround Time	**7 days (Gs)**	**6 days (Gs)**	**4 days (Gx)**	**3 days (Gx)**
	(AmpliSeq Panel - 400+ gene)	**(AmpliSeq Panel - 50+ gene)**	**(Oncomine OPA - 50+ gene)**	**(Oncomine OPA - 50+ gene)**

Gs: *GeneStutio/S5*

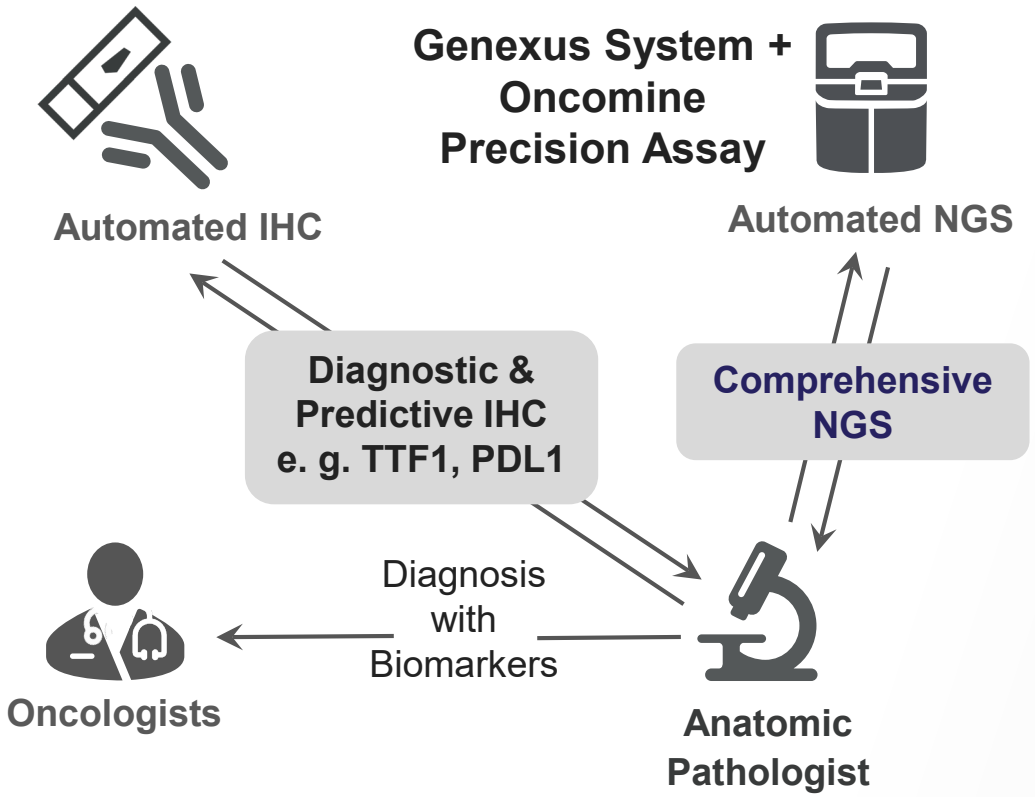
Gx: *Genexus System*

PCR amplicon-based genomic profiling enables effective and timely treatment selection for most cancer patients

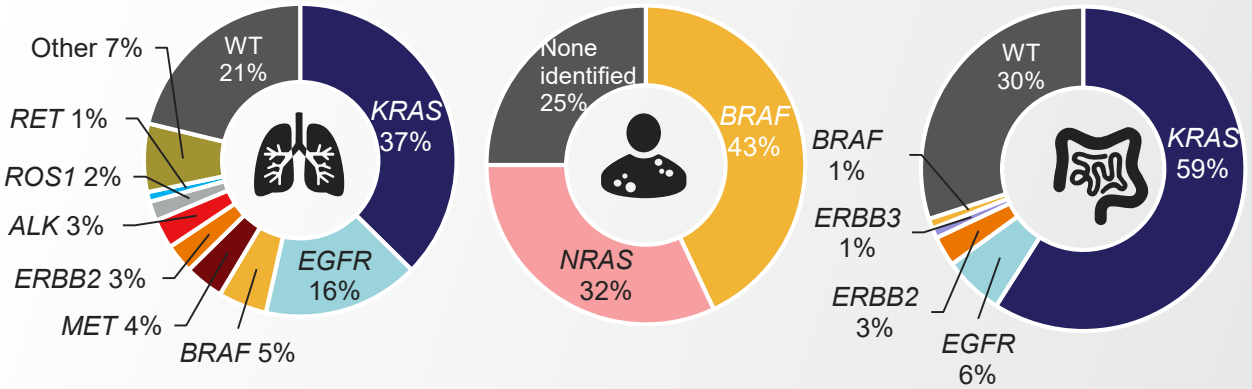
[1]Tomlins et al., *JCO* 2022, doi:10.1200/PO.20.00472; [2]Volckmar et al., *Int. J. Cancer* 2019, doi:10.1002/ijc.32133; [3]Matsumoto S. et al. JCO 2021 doi:10.1200/JCO.2021.39.15_suppl.9094; [4]Illié M., et al. Cancers 2022, doi:10.3390/cancers14092258)

Community-based rapid NGS to support cancer molecular testing

Point of care workflow



Distribution of genetic alterations



Median **TAT = 3 business days**

NGS provided an **incremental clinical utility in 18% of the cases**, defined as a result that would change systemic therapy prescription

Sheffield BS et al. Curr Oncol 2022 (doi:10.3390/curroncol29030113)

Introducing the Oncomine Dx Express Test (CE-IVD)

Fast results

Results can be generated in as little as 24 hours, enabling the integration with IHC results

Efficient use of samples

Requiring only 10 ng of DNA and RNA extracted from as little as two 5-micron FFPE slides, and a liquid biopsy option

End-to-end solution

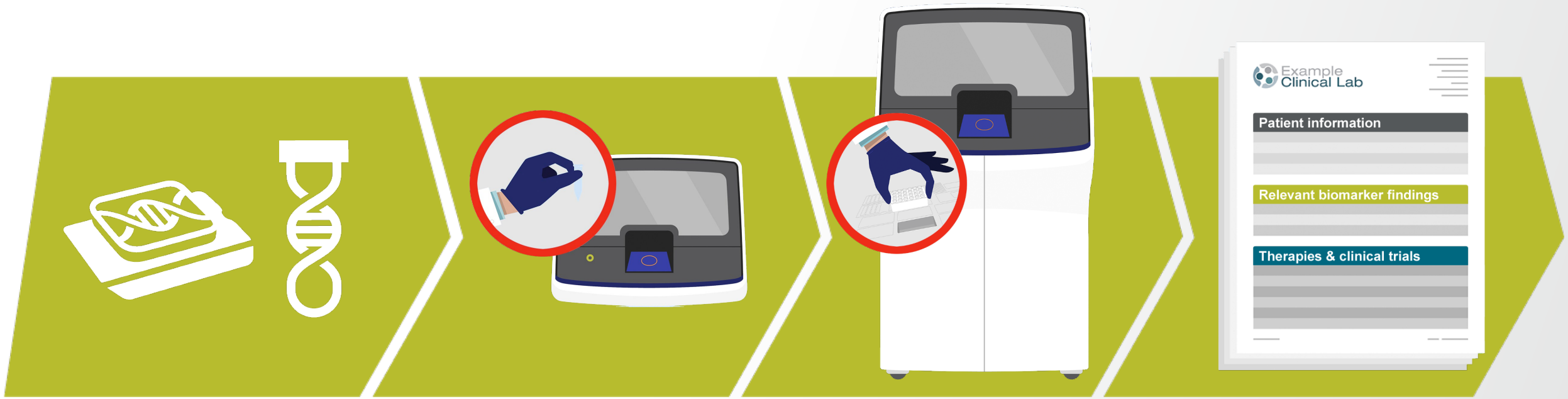
Automated nucleic acid extraction, library preparation, sequencing, and analysis

Full Clinical report

Reporting solution that provides sample–specific view of each biomarker matched to relevant evidence

Oncomine Dx Express Test sample workflow

Only 2 instruments, 1 software and **20 min hands-on** time to generate results in as little as **24 hours**



Patient sample

Nucleic acid extraction*

Library preparation, sequencing, and analysis

Report

*Purification instrument is not CE IVD

Oncomine Dx Express Test pan-cancer covers a wide range of clinically relevant biomarkers

DNA				RNA
Deletions, insertions, and substitutions			Copy number alterations	Fusions and splicing variants
AKT1	*ESR1*	*MAP2K2*	***AR*** 💊	*ALK* 💊
AKT2	*FGFR1* 💊	*MET* 💊	***EGFR*** 💊	***AR*** 💊
AKT3	*FGFR2* 💊	*NRAS* 💊	***ERBB2*** 💊	***BRAF*** 💊
ALK 💊	*FGFR3* 💊	*NTRK1* 💊	***ERBB3***	***ESR1***
AR 💊	*FGFR4*	*NTRK2* 💊	***FGFR1*** 💊	***FGFR1*** 💊
ARAF	*FLT3* 💊	*NTRK3* 💊	***FGFR2*** 💊	***FGFR2*** 💊
BRAF 💊	*GNAS*	*PDGFRA* 💊	***FGFR3*** 💊	***FGFR3*** 💊
CDK4 💊	*HRAS*	*PIK3CA* 💊	***KRAS*** 💊	*MET* 💊
CHEK2 💊	*IDH1* 💊	*PTEN*	***MET*** 💊	***NRG1*** 💊
CTNNB1	*IDH2* 💊	*RAF1*	***PIK3CA***	*NTRK1* 💊
EGFR 💊	*KEAP1*	*RET* 💊		*NTRK2* 💊
ERBB2 💊	*KIT* 💊	*ROS1* 💊		*NTRK3* 💊
ERBB3 💊	*KRAS* 💊	*STK11*		***NUTM1***
ERBB4	*MAP2K1*	*TP53*		*RET* 💊
				ROS1 💊
				RSPO2
				RSPO3

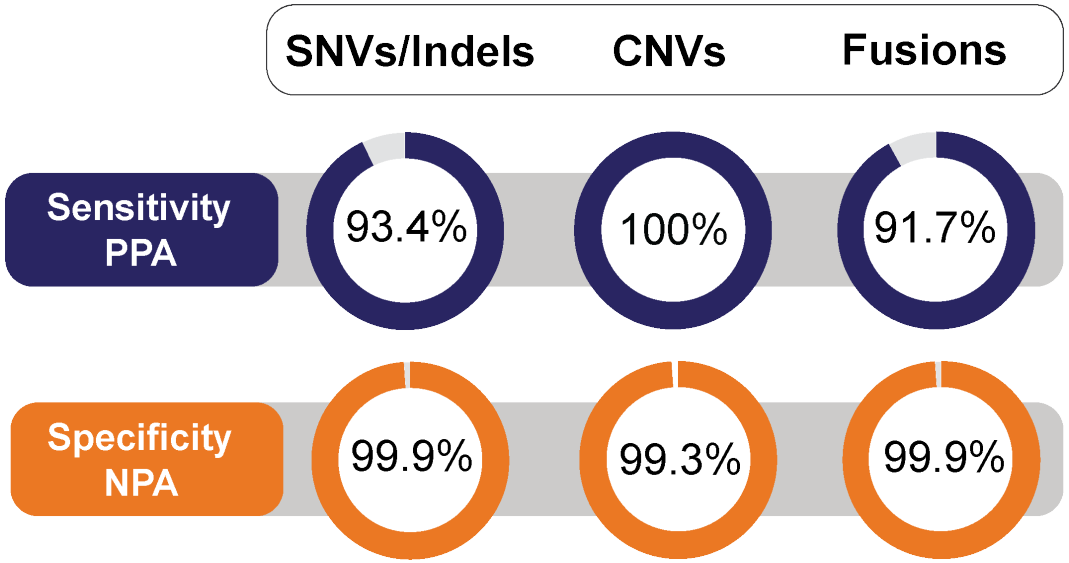
💊 FDA/EMA approved therapy

Genes in **bold** are only available for FFPE.

Fully validated CE-IVD solution for FFPE and plasma

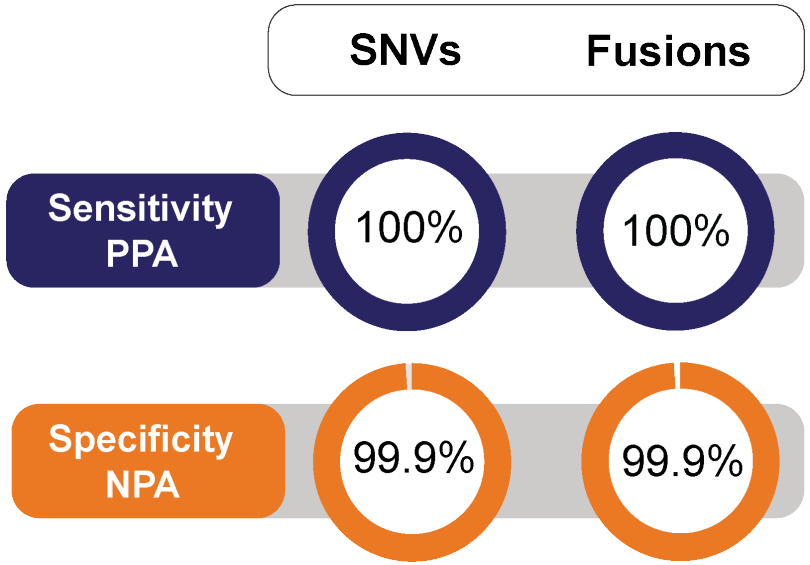
Analytical accuracy study

151 clinical FFPE tumor specimens from 6 cancer types (breast, colorectal, glioma, melanoma, NSCLC, and thyroid)



Analytical accuracy study

80 plasma specimens from patients with NSCLC (40 variant-positive and 40 variant-negative)



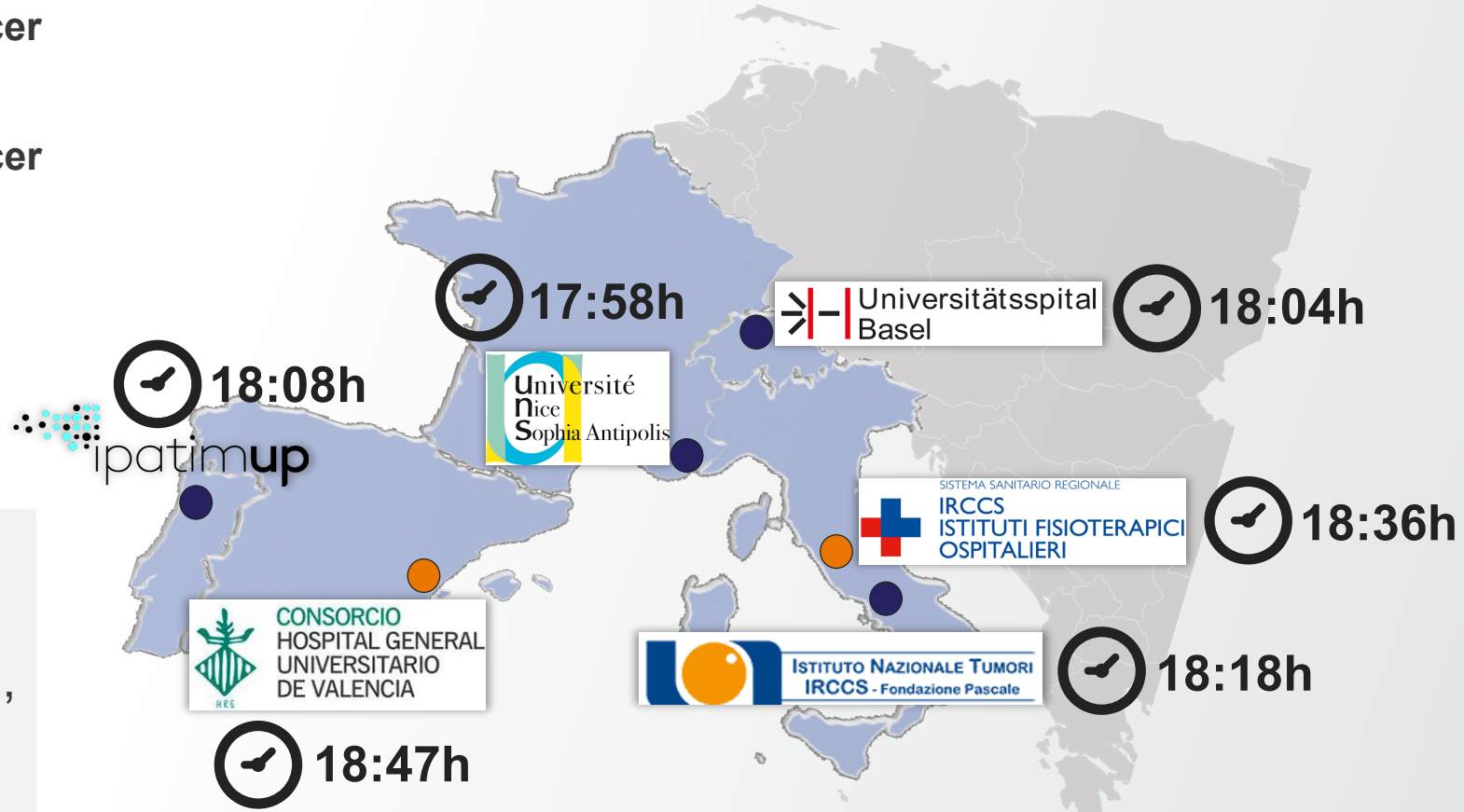
PPA = positive percent agreement; NPA = negative percent agreement

For complete details on studies and results, see the Oncomine™ Dx Express Test Part I: Test Description and Performance Characteristics User Guide.

ODxET evaluation at clinical lab sites across Europe

Genexus Purification System
Genexus Integrated Sequencer

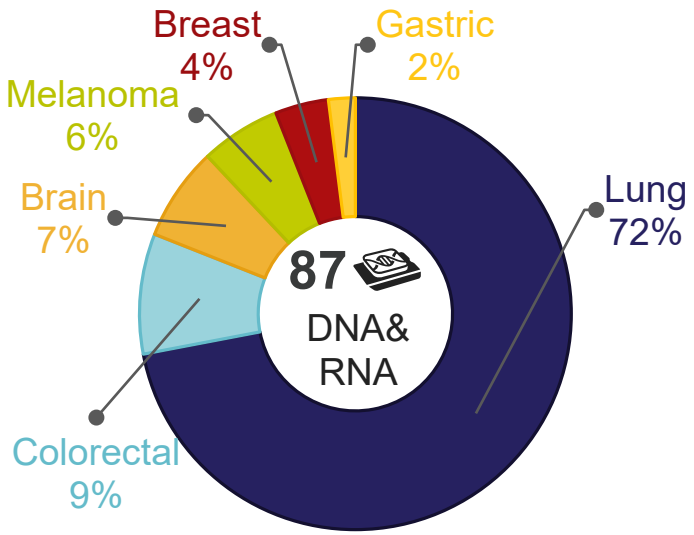
Genexus Integrated Sequencer

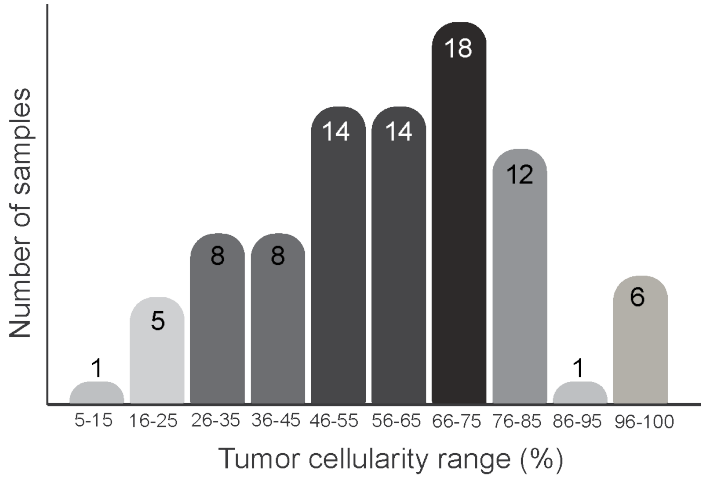


TAT (library, templating, sequencing, and analysis) among the sites was **18.3h**

Overview of the cohort of the analysed samples

Samples evaluated represent **a variety of cancer types** across **a range of tumor cellularity**





ALL ESCAT Tier IA, IB, IC for NSCLC represented and clinically relevant variants for other tumor types

NSCLC

I-A *ALK* fus, *EGFR* T790M, *EGFR* ex9del & L858R

I-B *BRAF* V600E, uncommon *EGFR*, *MET* ex14 skipping, *ROS1* fus

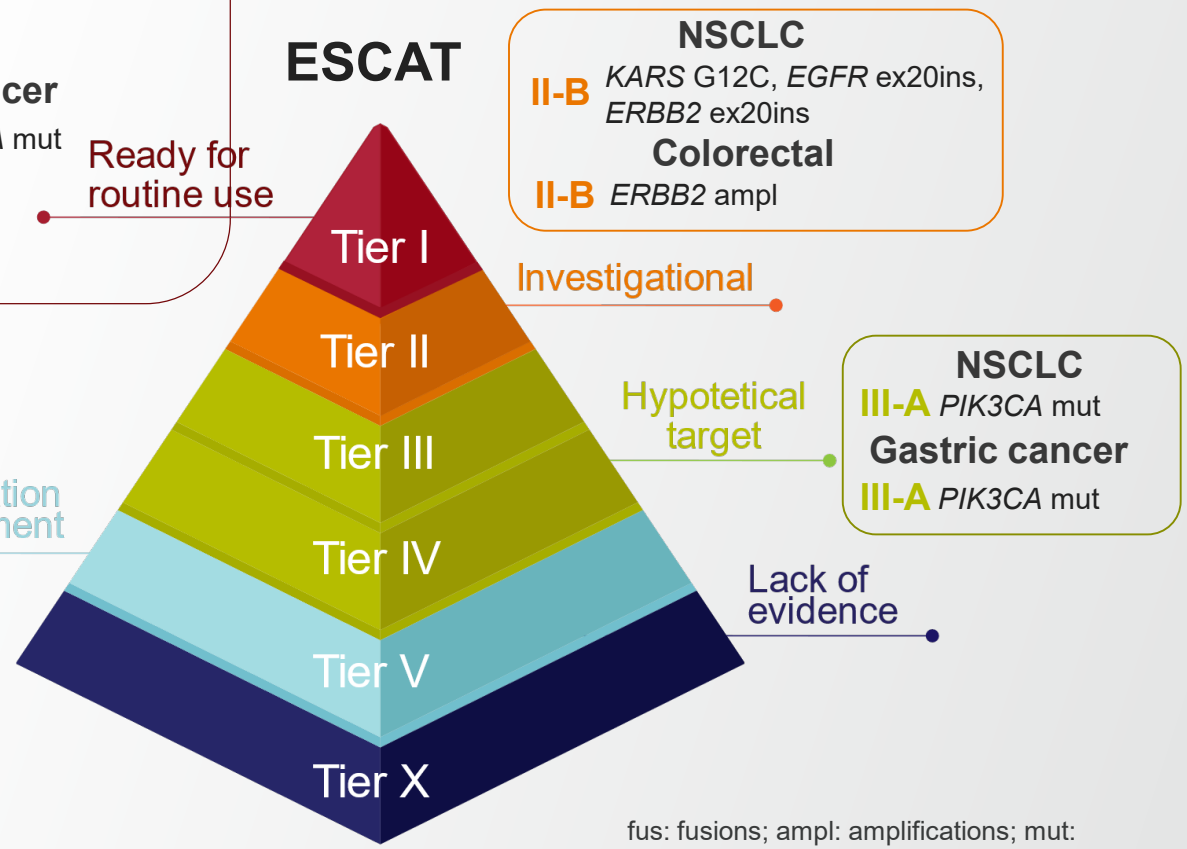
I-C *NTRK* and *RET* fus

Breast cancer

I-A *ERBB2* ampl, *PIK3CA* mut

Colorectal

I-A *BRAF* V600E



NSCLC

II-B *KARS* G12C, *EGFR* ex20ins, *ERBB2* ex20ins

Colorectal

II-B *ERBB2* ampl

NSCLC

III-A *PIK3CA* mut

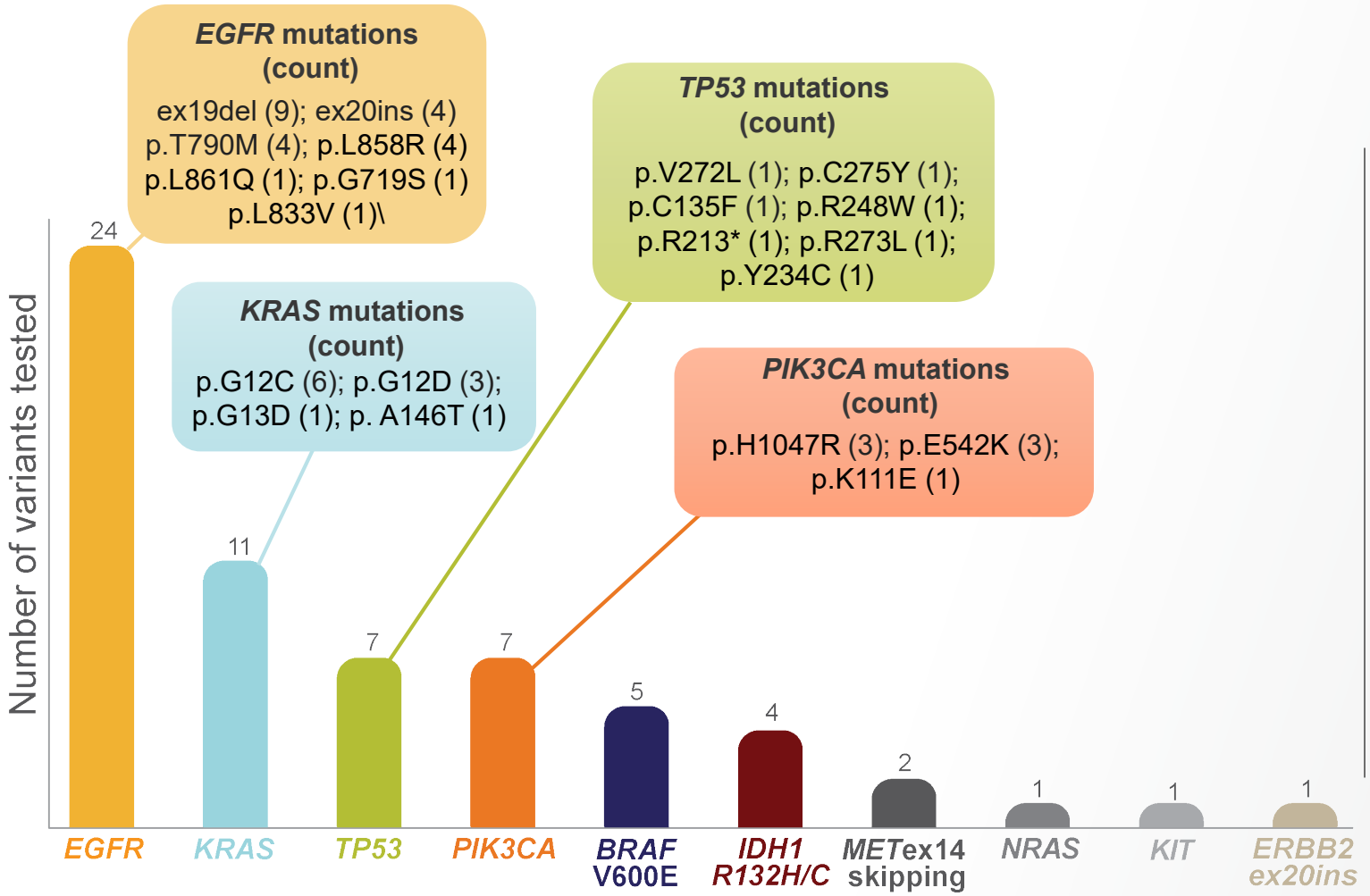
Gastric cancer

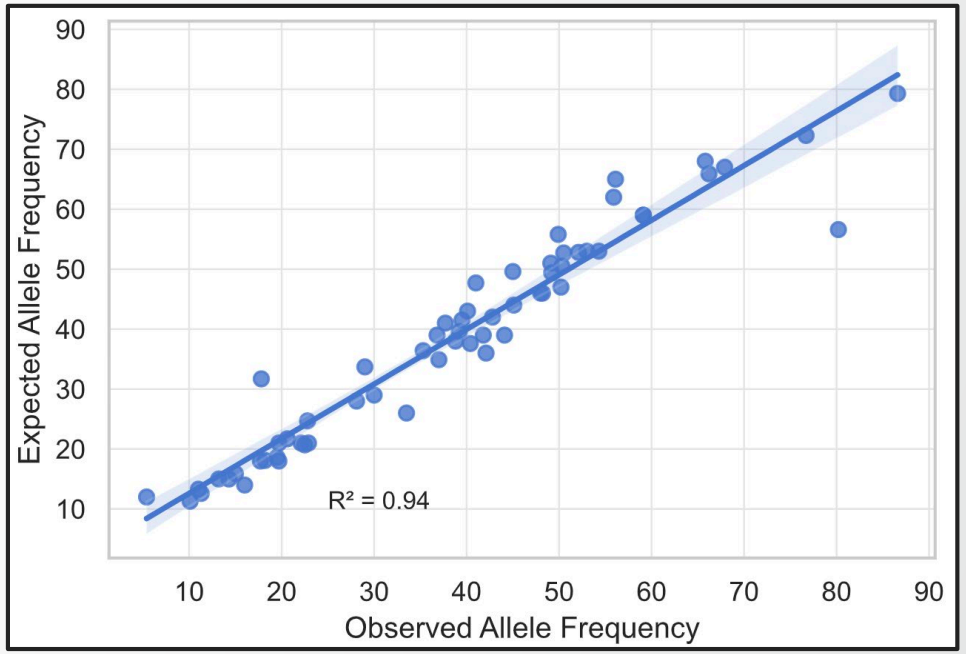
III-A *PIK3CA* mut

fus: fusions; ampl: amplifications; mut: mutations; ex: exon; ins: insertion, del: deletion

ODxET detects clinically relevant SNV and INDEL

High correlation of observed vs. expected allele frequencies of tested mutations





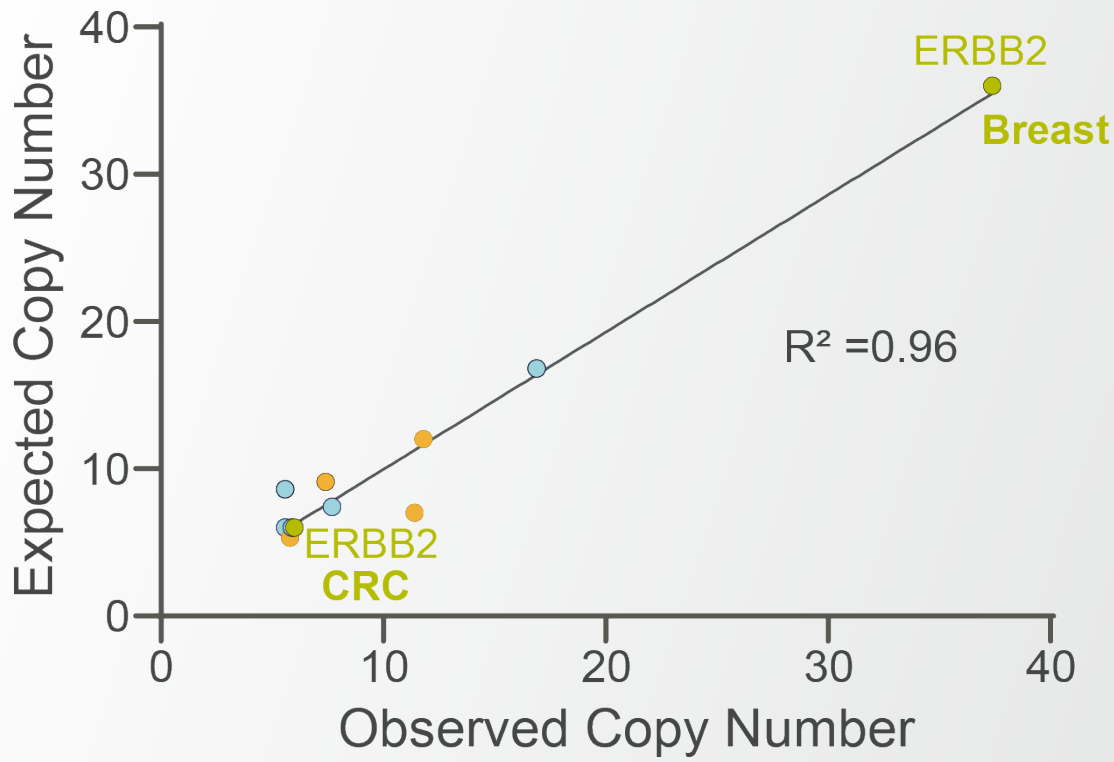
Strong correlation (R^2 = 0.94) between ODxET allele frequency measurement vs. pre-characterization

NOTE: Only mutations with pre-characterized testing information are included in the chart above

Since pre-characterized samples were selected for this evaluation, the prevalence of genes & variants above does not reflect what is found in literature

ODxET detects a wide range of copy number variations

Indication	Gene	Observed CN	Expected CN
Lung	EGFR	5.6	6
Lung	EGFR	5.6	8.6
Lung	MET	5.8	5.3
Breast	ERBB2	5.9	6
Lung	EGFR	6	6
Lung	MET	7.4	9.1
Lung	EGFR	7.7	7.4
Lung	MET	11.4	7
Lung	MET	11.8	12
Lung	EGFR	16.9	16.8
CRC	ERBB2	37.4	36
Lung	EGFR	5.6	6

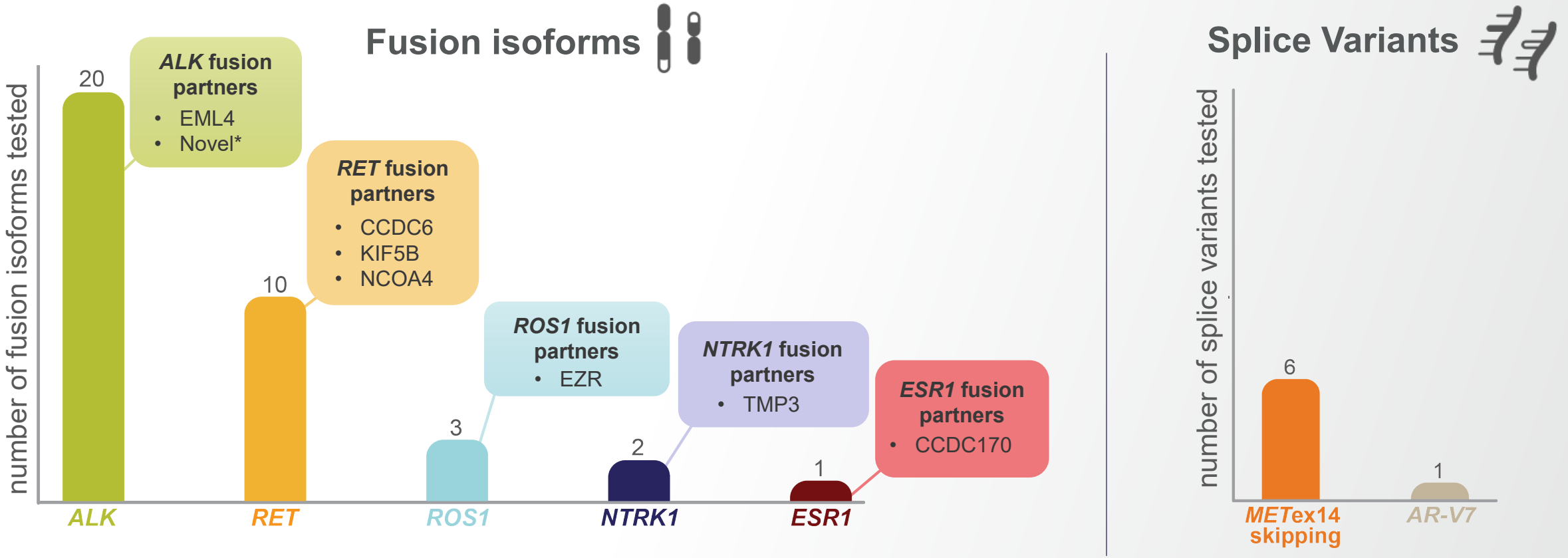


Strong correlation (R^2 = 0.96) between ODxET copy number measurement vs. pre-characterization

Pre-characterization assays include: Oncomine Precision Assay, Oncomine Focus Assay, INFORM HER2 FISH

NOTE: Only copy number amplification with pre-characterized testing information are included in the chart above

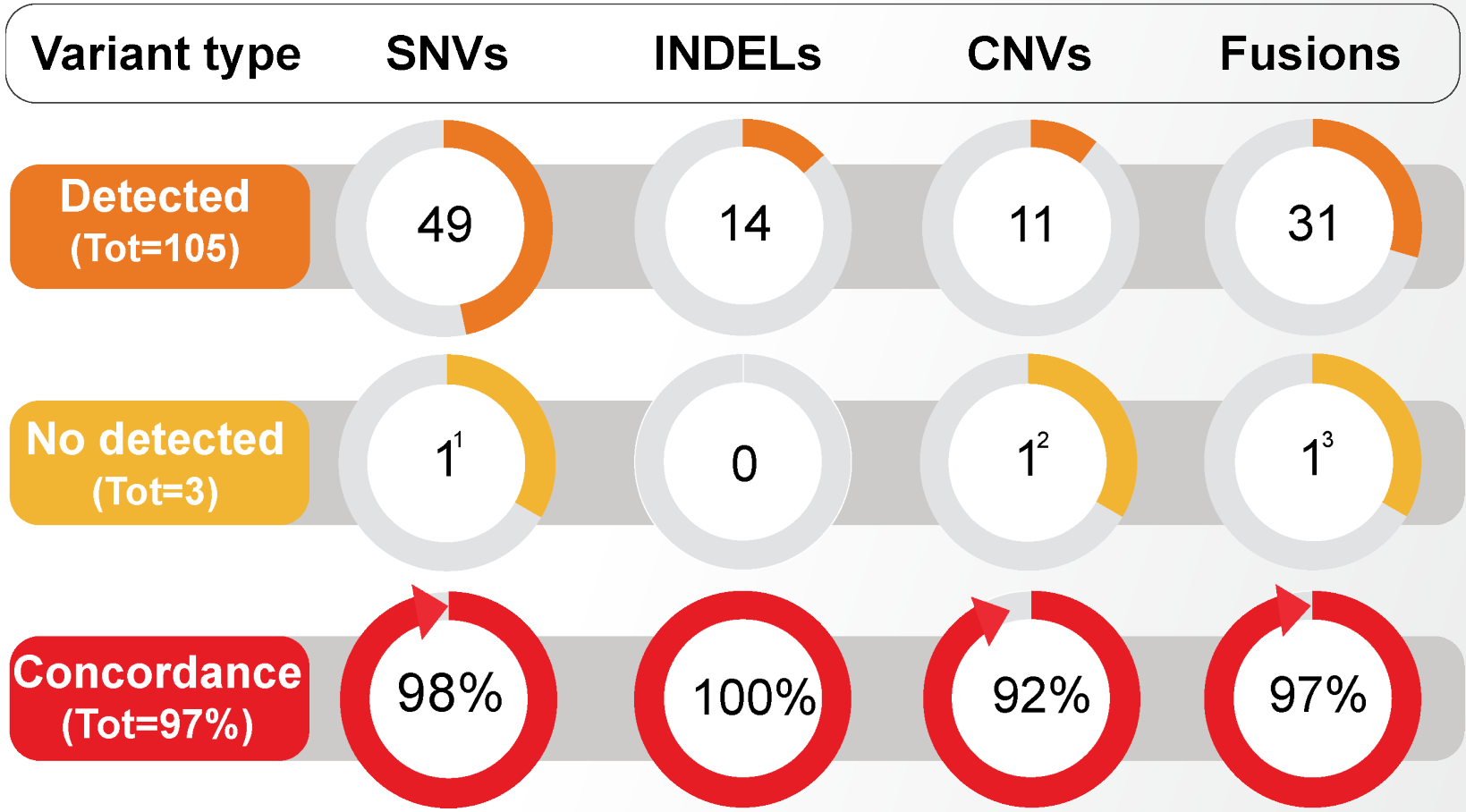
ODxET detects clinically relevant fusion isoforms and splice variants



- Exon tiling imbalance in ODxET enables the detection of **novel fusions**
- ODxET limit of detection for fusions & splice variants ranges from 6 to 5023 molecules

Pre-characterization assays include: Oncomine Precision Assay, Oncomine Focus Assay, Oncomine Comprehensive Assay v3, Archer Fusion Plex, FISH, Custom
**Novel ALK fusion identified with exon tiling imbalance and therefore partner gene is not known*
NOTE: Only fusions and splice variants with pre-characterized testing information are included in the chart above

High performance of ODxET across all variant types



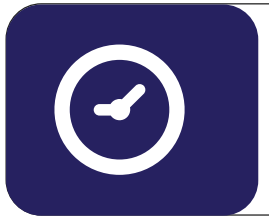
[1] Pre-characterization was done with plasma sample and liquid biopsy assay, where the original result had a co-mutation of EGFR exon 19 del and KRAS G12C. ODxET evaluation detected only the EGFR exon 19 del. Discordance can be due to specifics with the original test method (e.g., presence of KRAS G12C due to clonal hematopoiesis).

[2] Expected variant result not detected due to sample failure (i.e., suspected poor sample quality).

[3] Pre-characterized data had ALK fusion but not detected in ODxET testing. Further evaluation needed, given (1) demonstrated capability of ODxET to detect this specific ALK fusion isoform and (2) the high level of ALK fusion transcript level in the original sample.

Key Takeaways from Evaluation

The outcome of this evaluation demonstrated the following:



Genexus Dx Integrated Sequencer is automated and allows multiple biomarker detection with an **18 hours turnaround time** from nucleic acid to report

ODxET **simultaneously detects different types of clinically relevant cancer variants**, including SNVs, INDELs, CNVs and fusions

Cross validation among FFPE samples from EU clinical laboratory sites demonstrated that ODxET is highly reproducible and has a strong **correlation and concordance** with orthogonal methods

Thank you!

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Prof. Jose Carlos Machado – Ipatimup, Porto – Portugal
Dr Philp Jermann - Universitätsspital Basel, Basel – Switzerland