exacta®

The most comprehensive tumour investigation

Nordic Laboratories

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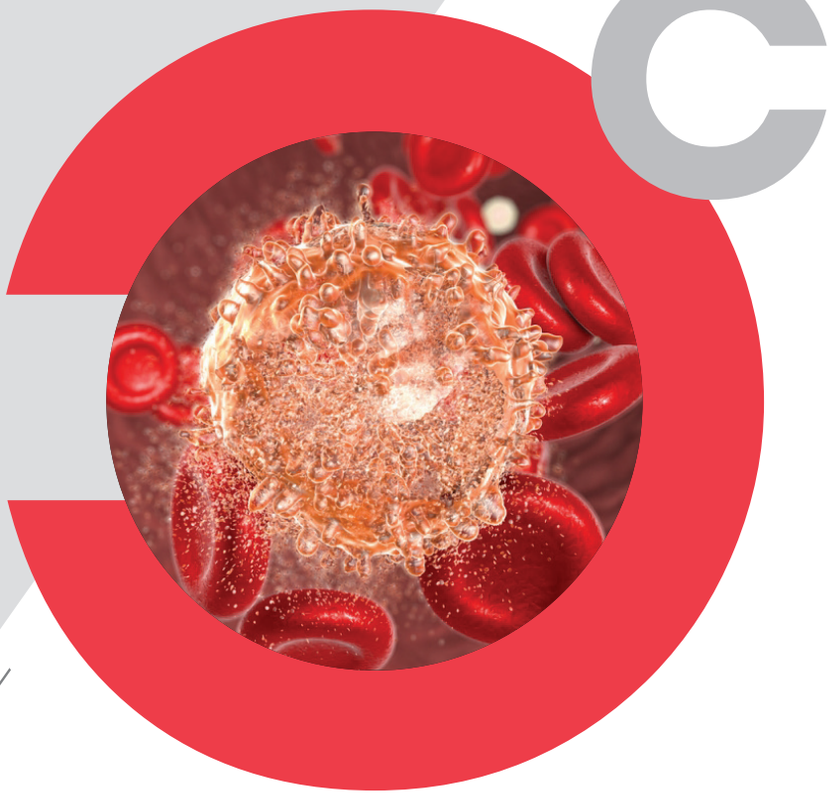


About exacta®

Every human being is different and unique, similarly ever person's cancer is unique. Conventional 'Standard of Care' approaches do not take into consideration molecular- genetic architecture of a particular patient's tumour. Consequently, patients could suffer due to failed therapies or aggressive relapse. It is, thus, imperative that the molecular architecture of the tumour is studied comprehensively before deciding the treatment plan, which has to be personalised to individual patients and their disease. exacta® is backed up by several published interventional trials showing significant advantages vs previous therapy regimens.

exacta® is a comprehensive in depth tumour analysis. It analyses 100's of millions of data points at the molecular level to reveal all possible targets for precision drugs.

exacta® helps unravel driver mutations and pathways that are propelling a person's cancer through multi-analyte and multi-coordinate analysis over 20.805 genes in the cancer genome.
This analysis helps identify drugs that would be most effective for a particular solid tumour. exacta®, thus enables a highly sophisticated treatment strategy beyond conventional perspective, even for difficult to treat or late stage cancers.

exacta® is particularly recommended for cancer patients where ...

... first-line therapy has failed.

... cancer has relapsed.

... cancer is high-grade / metastatic.

... newly diagnosed patients with difficult cancers such as stomach, oesophagus, pancreas, gall bladder, GIST etc.

... risk of therapy failure is high.

exacta® Methodology

Targeted Genes	SNVs, CNVs, Amplifications, Mutation burden, Germline mutations
RNA Sequencing	KEGG pathways (Disease, Actionable, Resistance)
Pharmacogenetics	Genotyping for CYP450, drug transporters for drug toxicity and efficacy
Chemosensitivity	In vitro cell based assay for testing drugs identified, including other recommended combinations
Liquid Biopsy	Mutation load, Tumour heterogeneity

exacta® Advantages

Most Optimal Targeted Therapy Selection:

- exacta® identifies possible molecular targets and cell cycle pathways to find the most appropriate molecular targets for targeted therapy.
- All relevant biomarkers for targeted therapy selection, including mutations, deletions, gene rearrangement, gene amplification / expression, are analysed.

Most Optimal Cytotoxic Therapy Selection:

- Cytotoxic drug response / resistance of cancer genome, based on DNA and gene expression.
- Comprehensive exacta® includes chemosensitivity testing for cytotoxic drug efficacy prediction.

Assessment of adverse drug reactions:

- Selection of therapy with least side effects based on analysis of germline mutations.

Therapy Recommendation (TR):

- Proprietary exacta® analysis provides best therapy combination option to treating physician.

Comprehensive exacta®

Parameters and Methods of Analysis	exacta®
Tumour DNA analysis	452 genes (tissue biopsy) 409 genes (liquid biopsy)
Mutations and Gene Amplifications	✓
Fusion / Rearrangements	51 genes (tissue biopsy) 12 genes (liquid biopsy)
Tumour Gene Expression	20.805 genes
Cellular pathways as per KEGG	✓
Chemosensitivity*	up to 100 drugs
Liquid Biopsy Cell free DNA (cfDNA)	✓
ICC Immunocytochemistry (mTOR, VEGFR, EGFR, etc.)	✓
Microsatellite Instability (MSI / MMR)	✓ (tissue biopsy / liquid biopsy)
Tumour Mutation Burden (TMB)	✓
Relevant IHC, PD-L1, AR etc.	✓ (tissue biopsy)
Circulating Tumor Cells (CTCs)	✓
Therapy Recommendations (TR)	✓
Pharmacogenetic Guidance	✓
Immunotherapy Guidance	✓
Sanger Sequencing to rule out germline nature of high MAF alterations	✓
Sensitive ddPCR assays to detect therapy relevant low MAF alterations	✓
Longitudinal Monitoring for MAF Comparisons of Repeat Tests	✓

*Subject to availability of adequate sample.

NGS: Next-Generation Sequencing
IHC: Immunohistochemistry
cfDNA: Cell Free DNA

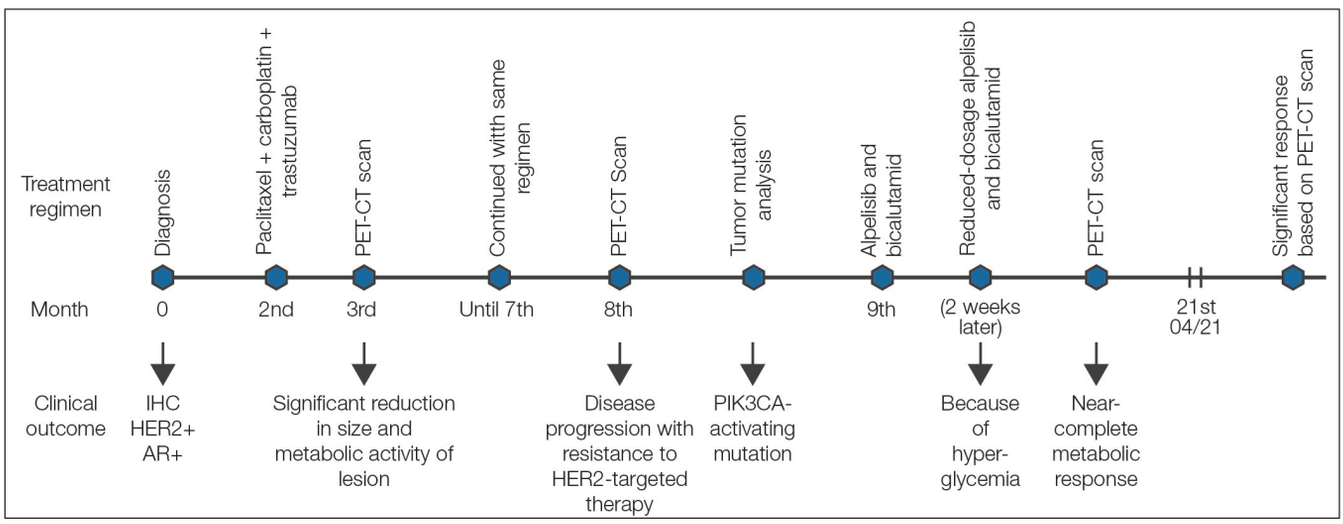
cfTNA: Cell Free Total Nucleic Acid
MAF: Mutant allele frequency
ddPCR: Droplet Digital PCR

CE: Capillary Electrophoresis
KEGG: Kyoto Encyclopedia of Genes and Genomes
ICC: Immunocytochemistry

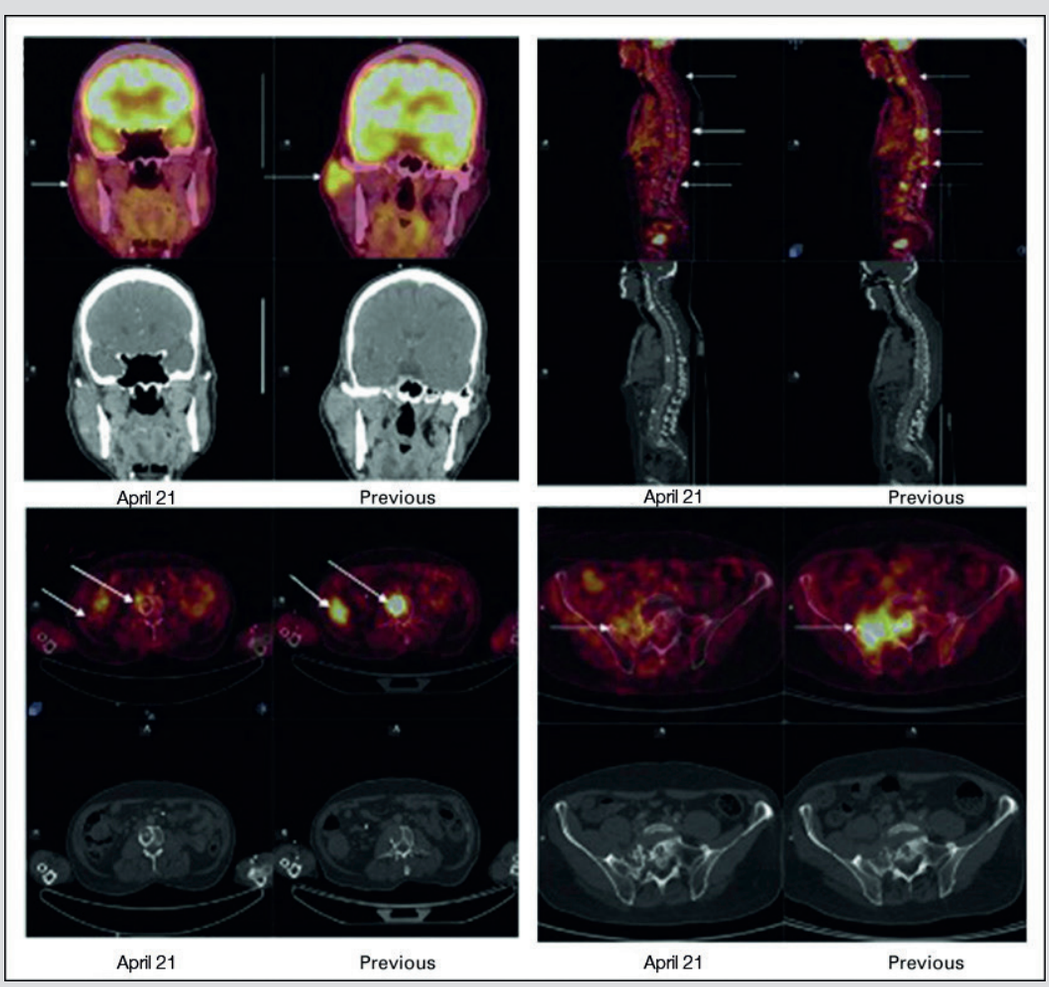
exacta®

Case Study I

Advanced salivary gland carcinoma, 64-year-old male patient



Result of the recommended therapy



Sheth H. et al. Excellent Response With Alpelisib and Bicalutamide for Advanced Salivary Duct Carcinoma With PIK3CA Mutation and High Androgen Receptor Expression-A Case Report. JCO Precis Oncol. 2021 May 3;5:PO.20.00436. doi: 10.1200/PO.20.00436.

Case Study – II

Stage IV Triple negative Breast Cancer
22 year old female patient

Clinical History

Aug ’16	**Diagnosis: Left Breast**
Aug – Jan ’16	Cyclophosphamide + Doxorubicin + Docetaxel
Nov ’16	Left Mastectomy
Feb – Mar ’17	Radiotherapy
May – Jun ’17	Methotrexate + Cyclophosphamide
Jun – Jul ’17	Everolimus
Jul ’17	**PET-CT: Progression**

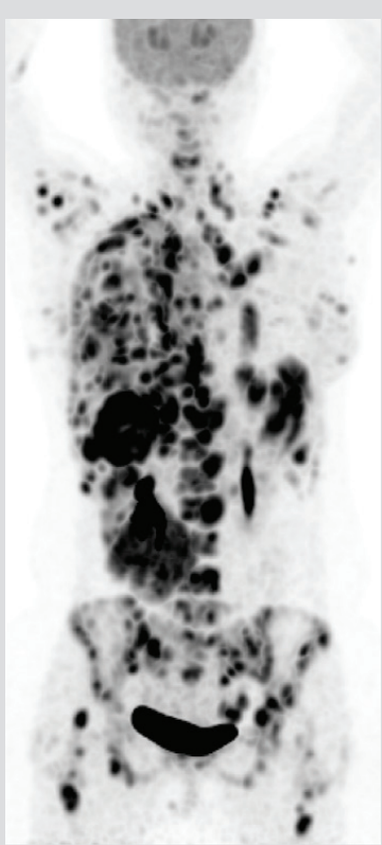
exacta® rationale for therapy selection

Gene / Pathway / Analysis	Feature	Therapeutic Implication
PDGFRA, KIT, KDR	Gain of Copy	Axitinib
Chemosensitivity	Cytotoxicity	Carboplatin Gemcitabine

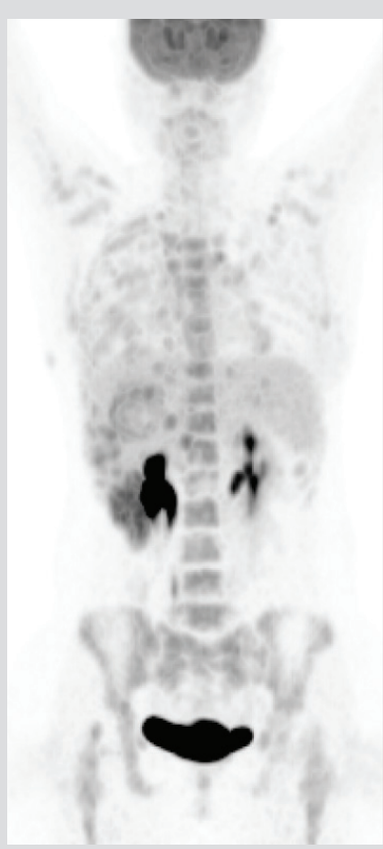
Benefit from exacta® – recommended therapy

before

Cancer had progressed following 5 lines of therapy.



day 0



after

Administration of exacta®: recommended therapy led to regression of cancer.

day 34

Publications

Crook, T., Gaya, A., et al. (2021) 'Clinical utility of circulating tumor-associated cells to predict and monitor chemo-response in solid tumors', Cancer Chemotherapy and Pharmacology, 87(2), pp. 197–205. doi:10.1007/s00280-020-04189-8.

Crook, T., Patil, D., et al. (2021) 'Angiogenesis Inhibitors in Personalized Combination Regimens for the Treatment of Advanced Refractory Cancers', Frontiers in Molecular Medicine, 1, p. 749283. doi:10.3389/fmmed.2021.749283.

Crook, T., Vaid, A., et al. (2019) 'mTOR Inhibitors in Combination Regimens Guided by Encyclopedic Tumour Analysis Show Superior Outcomes Compared to Monotherapy in Refractory Cancers', Annals of Oncology, 30 (Supplement_7):mdz413-115.

Nagarkar, R., Patil, D., et al. (2020) 'Encyclopedic Tumor Analysis for Guiding Treatment of Advanced, Broadly Refractory Cancers: Results from The RESILIENT Trial', Journal of Clinical Oncology 38, no. 15_suppl. published online May 25, 2020, DOI: 10.1200/JCO.2020.38.15_suppl.e15623.

Sheth, H. et al. (2021) 'Excellent Response With Alpelisib and Bicalutamide for Advanced Salivary Duct Carcinoma With PIK3CA Mutation and High Androgen Receptor Expression—A Case Report', JCO Precision Oncology, (5), pp. 744–750. doi:10.1200/PO.20.00436.

Akolkar, D.B., Patil, D., et al. (2021) 'Concordancy of Immunocytochemistry Profiling of Circulating Tumor Cells with Immunohistochemistry for Analysis of Therapeutically Relevant Biomarkers', Journal of Clinical Oncology 39, no. 15_suppl (May 20, 2021) 3047-3047. DOI: 10.1200/JCO.2021.39.15_suppl.3047 Journal of Clinical Oncology 39, no. 15_suppl (May 20, 2021) 3047-3047.

Sample requirement:

- 25 ml blood in DCGL and EDTA tubes
- Optional: 15 ml blood in DCGL and EDTA tubes as well as fresh tissue sample in DCGL transport media (4-6 cm^3 or 5 cores); alternative: FFPE tissue block

Turn Around Time (TAT):

- 10 to 14 days from receipt of the sample

FAQ's

If two patients have the same histopathological cancer type, and one of them undergoes exacta® analysis, can the other patient receive the same treatment as indicated in the TR of the first patient?

Just as each patient is unique, so is each cancer. No two patients' cancers are alike. Even two similar patients (e.g. age, gender, height, lifestyle) with the same type of cancer (e.g. lung) will have different molecular profile of tumours. Hence each patient should perform an individual exacta® test.

Why is it important to start treatment immediately?

Cancer can be very aggressive and may evolve rapidly; the tumour profile can change dramatically over time. Starting the treatment immediately is essential as it is the best strategy to counter the aggressiveness of the cancer. If there is a long enough delay the cancer may gain resistance to treatments and re-analysis may be required.

What kind of drugs will be recommended / given to the patient?

Only drugs that have been approved by the FDA will be recommended. These will include drugs that are FDA approved for use in same cancer / other cancer / other non-cancerous diseases. The TR will not recommend any investigational antineoplastic drugs / FDA-unapproved drugs.

Are there any follow-up molecular tests to assess the result of recommended therapy?

Liquid biopsy can be extremely beneficial for real-time patient monitoring because it allows modification of therapy as well as recurrence monitoring when the patient is in remission. So, precision oncology molecular tests (cancertrack™)will not only provide information for selection of therapy, but will also allow the oncologist to monitor the therapy in real time and make decisions that will benefit quality of life, overall survival and progression free survival.

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