exacta®

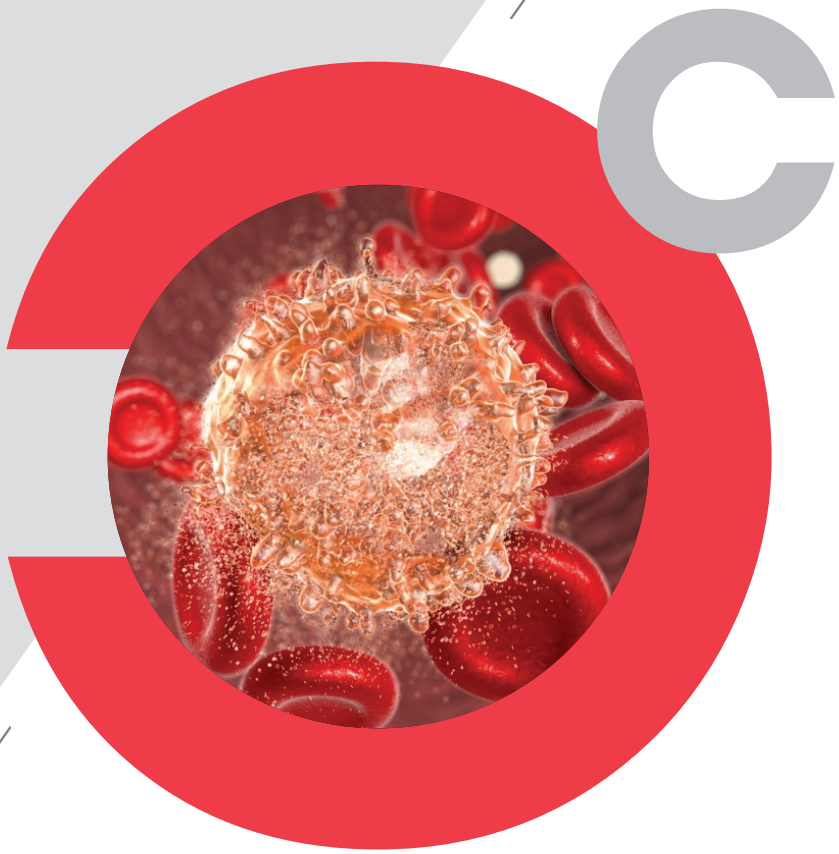
The most comprehensive tumour investigation

exacta®

ENCYCLOPEDIC TUMOUR ANALYSIS

ABSOLUTE IMPACT
ABSOLUTE SCIENCE
ABSOLUTE COMMON SENSE

DATAR CANCER GENETICS
UNITED KINGDOM | GERMANY | INDIA



About exacta®

Every human being is different and unique, similarly ever person's cancer also is unique. However, conventional 'Standard of Care' approach does not take into consideration the overall genetic architecture of a particular patient's tumour and consequently, patients could suffer due to failed therapies or aggressive relapse. It is, thus, imperative that the genetic 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 a comprehensive in depth tumour gene expression 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 the driver mutations and pathways that are propelling a particular person's cancer through multi-analyte and multi-coordinate analysis over 20.805 genes in the cancer genome. This analysis helps identify targeted drugs that would be most effective for a particular cancer. exacta®, thus enables a highly sophisticated treatment strategy beyond conventional perspective, even for difficult 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, Gene amplifications, Tumour mutation burden, Germline mutations
ICC Markers	e.g. mTOR, VEGFR1, VEGFR2, EGFR, VEGFA
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® Analysis Unravels

Most Optimal Targeted Therapy Selection:
exacta® molecular analysis for possible molecular targets and cell cycle pathways to identify 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. Confounding impact of simultaneous resistant molecular alterations on sensitizing mutations giving better therapy selection than single gene test based therapy.

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.

Drug Toxicity / Adverse Drug Reactions:
Selection of therapy with minimal side effects and best tolerance based on germline drug metabolizing enzyme (DME) response for likely drug toxicity / ADR prediction.

Drug Repurposing:
With recurrent or high grade cancer which has progressed despite therapy. exacta® can explore all possible therapeutic options by analysing all molecular alterations.

Longitudinal Disease / Therapy Monitoring:
Comprehensive exacta® enables effective tumour burden monitoring, therapy response monitoring and helps detect early therapy failure or recurrence.

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) 411 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*	> 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)	✓
Platforms	NGS, Microscopy, Arrays, ddPCR, CE
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	✓
Limit of Detection (MAF)	2.5 % (Tissue), 0.1 % (cfTNA)
Sensitivity at 0.1 % MAF (cfTNA)	97.06 %
Sensitivity at 2.5 % MAF	96.43 %
Positive Predictive Value	100 %

*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

Comprehensive exacta®

100s of Millions of Data Points Analyzed
(from Peripheral Blood and/or Fresh Tissue and/or FFPE Block / or Liquor)

Cell Free DNA

Exosomal 20.805 mRNAs

Driver Mutations; Rearrangements;
Insertions and Deletions from 452/411 genes

Direct Live Tumour Cell Assessment

Tumor Cell Cycle Pathways;
Identification of Drugs with/without Benefit

+

Artificial Intelligence/Database based,
multi-level iterative algorithm to determine optimum
(most favorable + least toxic) drugs and drug combinations

=

Clear, Unambiguous Clinically Actionable Therapy Recommendations

Sample requirement:
- 25 ml blood in DCGL tube and EDTA tube both
- Optional: 15 ml blood in DCGL tube and EDTA tube both as well as fresh tissue sample in DCGL transport media (13cm or 5 cores); alternative: FFPE tissue block

Turn Around Time (TAT):
- Analysis based on fresh tissue and blood – 8 to 10 days from receipt of the sample
- Analysis based on FFPE blocks and blood – 10 to 14 days from receipt of the sample

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Case Study – I

Stage IV Melanoma
57 year old male patient

Clinical History

Jan ’16	**Diagnosis: Malignant Melanoma**
Aug ’16	Ungual Lesion Excision
Dec ’16	**PET-CT, USG: Progression** Lymph Node Excission
Jan – Feb ’17	Radiotherapy
Mar ’17	Lymph Node Excision
Mar ’17	**PET-CT: Progression**

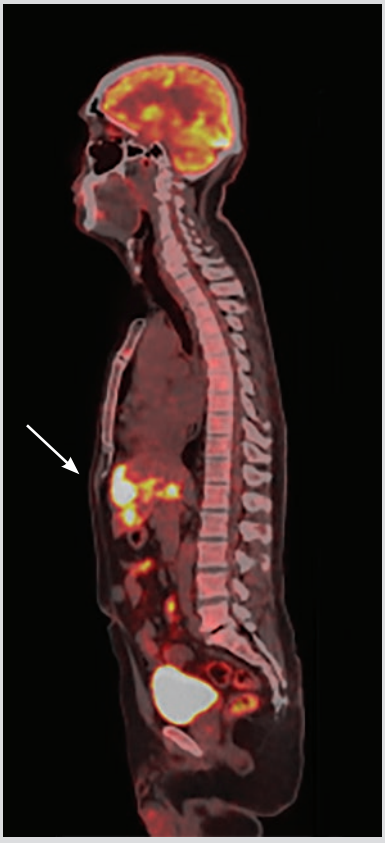
exacta® rationale for therapy selection

Gene / Pathway / Analysis	Feature	Therapeutic Implication
KIT, PDGFRA	Overexpression	Imatinib
TYMS	Overexpression	5-Fluorouracil
MMP	Overexpression	Doxycycline
EMT, MET	Upregulation	Atorvastatin
WNT	Upregulation	Quercetin
Cell Cycle	Upregulation	Curcumin
AR	Positive (IHC)	Bicalutamid

Benefit from exacta® – recommended therapy

before

Cancer had progressed following 4 lines of therapy.



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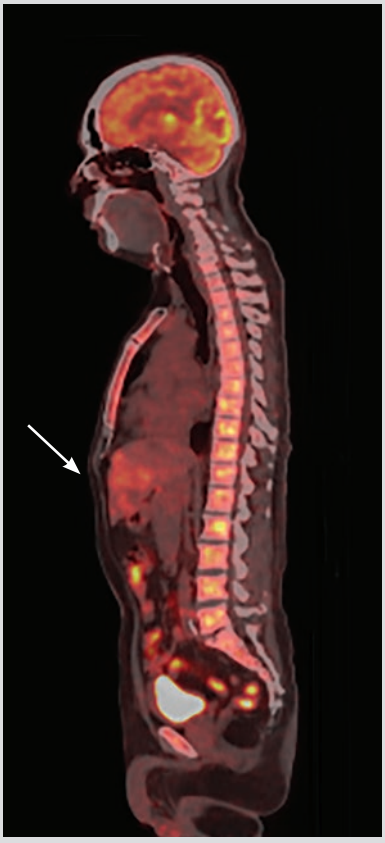


after

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

day 31

Case Study – II

Stage IV Invasive Ductal Carcinoma of Breast (TNBC*)
22 year old female patient

Clinical History

Aug ’16	**Diagnosis: IDC 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**

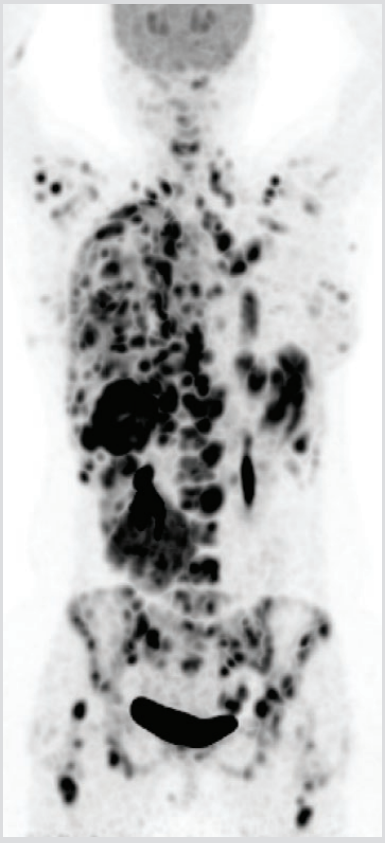
exacta® rationale for therapy selection

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.



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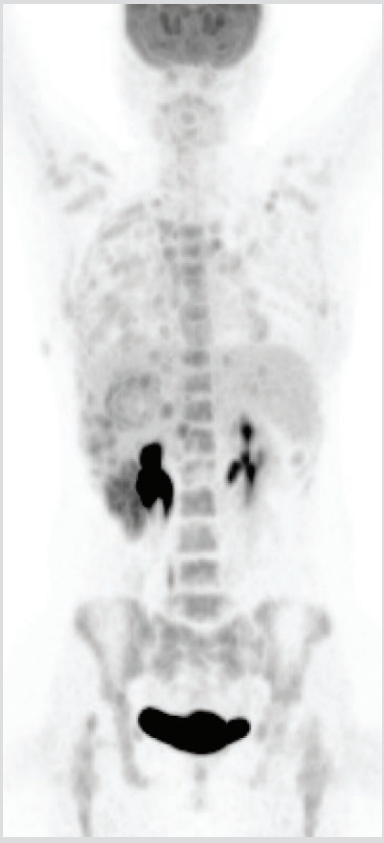

after

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

day 34

*TNBC: Triple negative breast cancer

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FAQ's

What is Therapy Recommendation (TR)?

TR is a document that lists the various drugs (single drugs or drugs in combination) found to be beneficial for the patient based on detailed analysis of multiple biomarkers which is carried out during exacta® analysis. TR is given as part of the exacta® report. Based on the established efficacy and safety profile, these drugs are assigned a preference list. Where drug combinations may work better than single drugs, these will be indicated.

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?

It is not advisable to do that. 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 receive a unique TR.

How is the TR used?

Therapy, based on the recommendations in TR, must be selected by the treating oncologist after suitability of the treatment has been determined as well as health and fitness of the patient have been evaluated. The selected treatment must be administered only under the supervision of the treating oncologist. The TR is only a list of drugs that have high potential for success and benefit to the patient. It is not meant as a prescription. TR is only a recommendation.

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 and be administered. 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 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, progression free survival.

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

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ISO 27001:2013

ISO 9001:2015

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