Smart Data in Oncology

Hasso Plattner Institut Potsdam

1st June 2017
Oncology – A Leading Topic in Heidelberg

EXCELLENCE in

- Clinical Translation and Basic Research
- Clinical and Translational Cancer Programs
- Interdisciplinary Patient Care
NCT 1.0 – Principles & Practice

Creating Interdisciplinarity
NCT 2.0 – New Building & Structures

IDENTITY & VISIBILITY
NCT 3.0 – The Next Level

DELIVER
Precision Oncology

EXCEL
Clinical and Translational Cancer Programs

GROW
Building Partners

SCIENTIFIC & CLINICAL EXCELLENCE
NCT 3.0 - Strategic Aims

• Position NCT as a Leading Comprehensive Cancer Center in Europe

• Expand NCT Precision Oncology Program

• Deliver at the Point of Care
  Translation – Personalization – Precision

• Expand Internationally Recognized Clinical Cancer Programs & Profile Areas

• Employ Novel, Innovative Treatment Concepts
FUNDING
New Research Building
CCC Building funded by DKH

PROFILE AREAS / RECRUITMENTS
- Innovative Medical Oncology
- Translational Research
- Radioimaging
- Theragnostics
- Link-up DKFZ HIPO, NCT POP & NCT MASTER
- Immunotherapy
- Systems Biology
- Multidisciplinary Profile Areas
NCT 3.0 - Profile Areas to be Expanded

**DELIVER**
- NCT Precision Oncology
- Novel, Innovative Treatment Concepts
- Clinical Trials & Biobanking Infrastructure/Expertise

**EXCEL**
- Molecular Stratification
- Immunotherapy
- Profile Areas - Neurooncology, Pancreatic Cancer, Radiooncology, Lung Cancer, Prostate Cancer
- NCT OncoCheck-Programm
- Innovative Oncological Imaging
- Molecular Tumor Pathology
- Biomarker Platform
- NCT DataThereHouse & Cancer Registry
- New Programs – CardiOncology, Palliative Oncology, Hematology
- NCT Basic Research Pipeline

**GROW**
- Partnerships
- Funding Programs
- Recruitment
- Talents
- Facilities
# NCT Precision Oncology Program

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**NCT DataThereHouse**
Organized in SAP HANA

**NCT OMICS**

| PATIENT ADMISSION – DOCUMENTATION - BANKING |
NCT DataThereHouse

Display Data from Various Sources for a Comprehensive Overview of Information Relevant for Personalized Treatment

**SEQUENCING DATA**

**ARRAY DATA**

**CLINICAL PATHWAYS**

**UNSTRUCTURED DATA**

**INDIVIDUALIZED TREATMENT PLAN**

**PHYSICIAN**

**SCIENTIST**

**TUMOR BOARD**

**CASE MANAGER**

**STUDY NURSE**

**DOCUMENTALIST**
NCT DataThereHouse

Current Scenario

- **REPORT**
- **REPORTER**
- **KIS, PACS, REGISTER**
- **PHYSICIAN**
  - **SCIENTIST**
  - **SOP**
- **BOARD**
- **EINBINDUNG**
- **NEUE STUDIE**
  - **EINSCHLUSS & AUSSCHLUSS KRITERIEN**
  - **STUDIEN PROTOKOLL**
  - **STUDY NURSE**
  - **SOP**
- **SPRECHSTUNDE/AMBULANZ**
- **KIS, PUBMED, UPTODATE, BIOBANK, INTRANET, REGISTER**
- **HYPOTHESE**
  - **LOI**
- **SCRIPTING**
- **BDT**
- **KONFERENZ**
  - **DOKUMENTAR**
  - **ARZT**
  - **FORSCHER**
- **BEGLEITENDE DIENSTE**
- **THERAPIE**
  - **AM NCT ODER EXTERN**
- **PATIENT**
- **PATIENTENPFAD**
  - **ABLAUF**
  - **DATENFLUSS**
  - **KONFERENZ**
  - **DATENBANK**
  - **PATIENTENAKTE**
NCT DataThereHouse

NCT Clinical Development Strategy

IS-H, PUBMED, UPTODATE, BIOBANK, INTRANET, IS-H, PACS

Organized in SAP HANA

IS-H, PUBMED, UPTODATE, BIOBANK, INTRANET, IS-H, PACS

NCT CANCER REGISTRY

PATIENT

ARZT

DIAGNOSE

THERAPIE AM NCT

KLINISCHE STUDIEN

FORSCHER

PUBLIKATION

DOKUMENTAR

FORSCHER

MONITORING

CANCER REGISTRY

NCT DataThereHouse

NCT Clinical Development Strategy

IS-H, PUBMED, UPTODATE, BIOBANK, INTRANET, IS-H, PACS

Organized in SAP HANA

PATIENT

ARZT

DIAGNOSE

THERAPIE AM NCT

KLINISCHE STUDIEN

FORSCHER

PUBLIKATION

DOKUMENTAR

FORSCHER
NCT MASTER Workflow

PATIENT ADMISSION
ENROLLMENT
CLINICAL DATA

DIAGNOSIS &
SAMPLING

NCT OMICS

BIOINFORMATICS
CLINICAL REPORT

MOLECULAR
TUMOR BOARD

INDIVIDUALIZED
THERAPY &
TRIALS

RESPONSE
RESISTANCE
PREVENTION

NCT DataThereHouse (SAP HANA)
NCT MASTER – Registry & Interventional Trial

Patient Sample Asservation → Sequencing → Bioinformatic Analysis → Clinical Evaluation → Validation → Molecular Tumor Board*

Unbiased Functional Testing → Focused Functional Testing

Feed Back Results Adapt Treatment/ Functional Testing

Basket Trial with Pathway Programs

PI3K-AKT-mTOR
RAF-MEK-ERK
Tyrosine Kinases
Developmental Pathways
DDR Signaling
Hypermutated/Immunotherapy

Stefan Fröhling, Christoph Heining, Hanno Glimm, Stefan Gröschel, Claudia Scholl (Functional Genomics)
DKTK – LMU München, Frankfurt, Dresden, Essen/Düsseldorf, Freiburg, Berlin
NCT MASTER – Registry & Interventional Trial

CURRENT STATUS

Entities

Recruitment (May 2016)
Metastatic gallbladder carcinoma
• Peritoneal and cutaneous metastasis during adjuvant chemotherapy with oxaliplatin/gemcitabine

Amplification of chromosome 17q12, including \textit{ERBB2}
• Outlier \textit{ERBB2} mRNA expression
• \textit{ERBB2} protein expression by immunohistochemistry (3+ according to ASCO guidelines)

Dual \textit{ERBB2} blockade: trastuzumab/pertuzumab

Complete remission for >12 months

Czink et al. Z Gastroenterol 2016
35-year-old patient with bladder tumor, bilateral pulmonary masses, enlarged hilar lymph nodes, and disseminated bone lesions.
- Histology inconclusive
- Refractory to cyclophosphamide, doxorubicin, vincristine, and prednisone

Co-existence of HRAS p.Q61R and BRAF p.F595L within single clone

Mutational spectrum highly suggestive of non-Langerhans histiocytosis

Rationale for MAPK pathway blockade using sorafenib or MEK inhibitor

No rationale for vemurafenib or dabrafenib due to risk of paradoxical MEK/ERK activation

Kordes et al. Leukemia 2016
Loss of phosphorylated ERK expression in tumor cells after 3 weeks of sorafenib and interferon alpha treatment

Frequent coexistence of intermediate-activity BRAF mutations and oncogenic RAS in various cancers
Wan et al. Cell 2004
COSMIC database

Rationale for Experimental Targeted Treatment

Physiologic BRAF signaling

BRAF<sup>F595L</sup> signaling in the absence of RAS activity

Collaboration between mutant HRAS and BRAF<sup>F595L</sup>

Cooperative activity of BRAF p.F595L and HRAS p.Q61R in aggressive histiocytic sarcoma

Kordes et al. Leukemia 2016
Development of a common path for clinical cancer genome sequencing and molecular stratification within DKTK

Further development of strategies for clinical translation

Refinement and expansion of strategies for functional annotation
NCT Precision Oncology Program

Stratified Oncology

Clinical Evaluation / Trials

Target Exploitation

Target Characterization

Target Identification

Patient Admission Documentation Banking

Early Diagnosis, Risk Stratification, Individualized Therapy & Prevention

Researcher

Physician

Molecular Tumor Board

Patient

NCT DataThereHouse

Metabolomics

Proteomics

Genomics

Immunomics

Radio/Imaging

Biomaterials

Patient

Patient

Patient

Patient

Patient

Patient

Clinical Data
National High Throughput Sequencing Core Unit

ICGC
INFORM
NCT Precision Oncology Program

2009 2010 2011 2012 2015

ICGC Sequencing

Illumina xten Cluster

ICGC
International Cancer Genome Consortium

dkfz.
NCT POP
Deutsches Konsortium für Translationale Krebsforschung

hipo

Applied Bioinformatics

OneTouchPipeline

PRIMIARY ANALYSIS
- fastq QC
- alignment
- duplicates
- lane merging
- calculate coverage
- genotype matching

SECONDARY ANALYSIS
- Pathogen integration
- Ploidy prediction
- INDELs
- SNVs
- Copy number variants
- Structural Variants
- Mutation in RNAseq?
- Mutation annotation

TERTIARY ANALYSIS: "INTERPRETATION"

RNA sequences

DNA sequences

Benedikt Brors

Pathogen integration

Mutation in RNAseq?

Mutation annotation

Structural Variants
INFORM = INdividualized therapy FOr Relapsed Malignancies in childhood

Feasibility-Registry Study (Year 1+2)

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<tr>
<th>ALL</th>
<th>AML</th>
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<tbody>
<tr>
<td>HGG (incl. DIPG)</td>
<td>Medullo/Ependym.</td>
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<tr>
<td>Ewing Sarcoma</td>
<td>Neuroblastoma</td>
</tr>
<tr>
<td>NHL</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>Rhabdoid Tumors</td>
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Clinical Trial (Year 3-5)

Enrollment

- Standard of Care: Backbone Chemotherapy
- Backbone
- Targeted Drug 1
- Targeted Drug 2

Angelika Eggert  Olaf Witt  Peter Lichter  Stefan Pfister
Big Data in Oncology for personalized medicine…

- needs to RETHINK the old & the new
- needs SMART Data
- is a TEAM Effort
NATIONAL CENTER FOR TUMOR DISEASES

NCT HEIDELBERG

THANK YOU