COCIR Annual General Assembly

Value of Genomics in the Context of Lung Cancer

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dkfz.
GERMAN
CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION
Research for a Life without Cancer

In the course of a lifetime, 1 person in 2 develops cancer, almost 1 person in 4 dies of cancer

Germany 2014

Overall population: 81.2 M

Life expectancy: 81 years

Prevalence: 1.6 M

New cases per year: 0.48 M

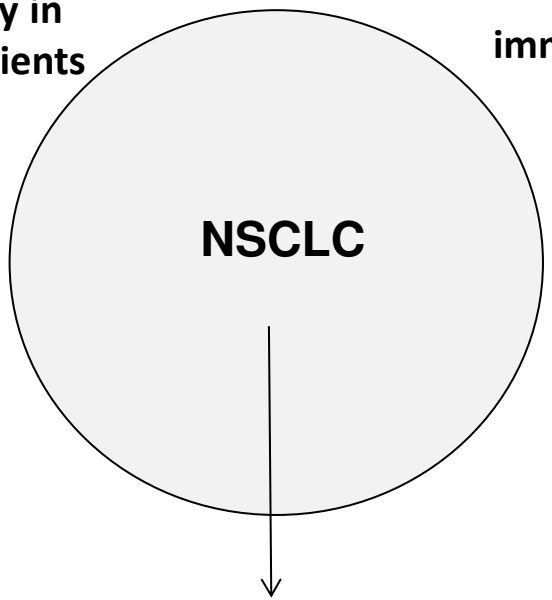
Mortality per year: 0.22 M

Develops cancer

Develops and dies of cancer

Systemic cancer therapy turns into personalized therapy: example non-small cell lung cancer (NSCLC)

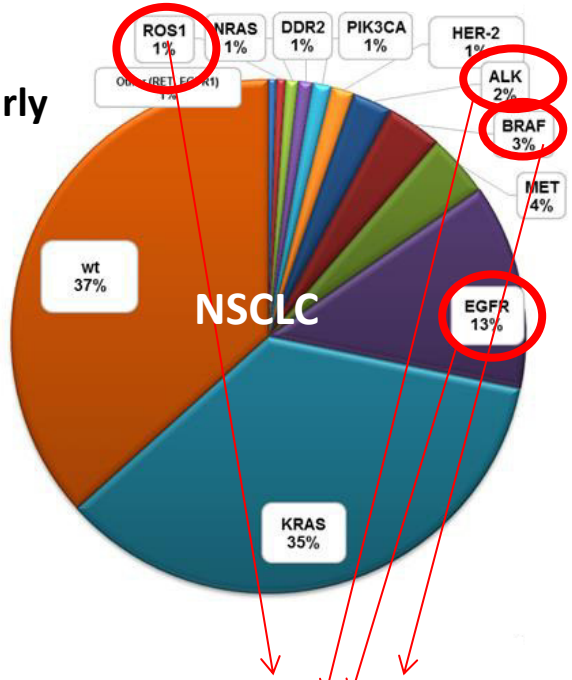
10 years ago:
chemotherapy in unselected patients



response rate: 20-30%

med. survival: 1 year

today:
targeted therapy (and immunotherapy) in molecularly selected subgroups



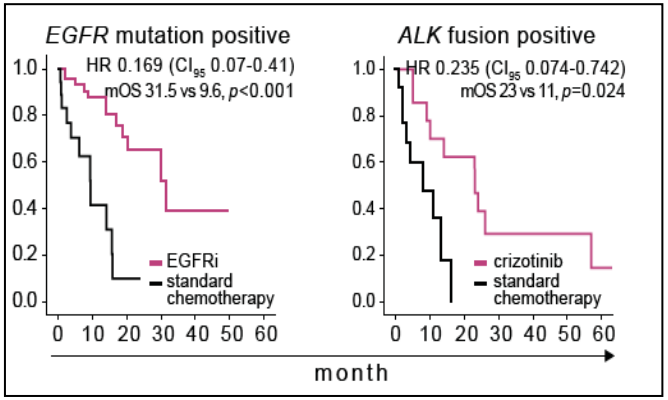
response rates: 60-70%

med. survival 5 years and more

better tolerability

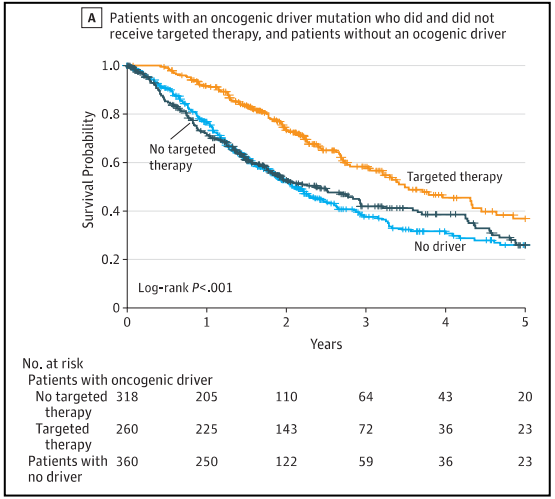
Personalized treatment prolongs survival substantially
Registry data

Germany:
Network Genomic Medicine



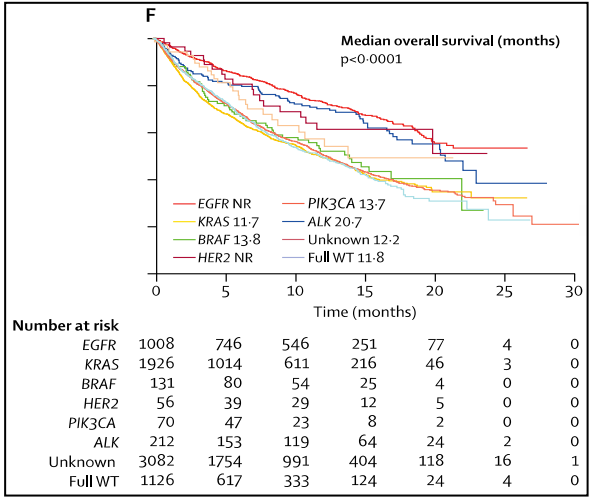
The Clinical Lung Cancer Genome Project and Network Genomic Medicine. Sci Transl Med 2013;5:209ra153

USA:
Lung Cancer Mutational Consortium



Kris et al. JAMA 2014;311:1998-2006

France:
INCA cohort



Barlesi et al. Lancet 2016;387:1415-26

ROS1 self-help group: molecular testing, off-label treatment and clinical trials save lives

Bärbel Söhlke
http://ros1-krebs.de/
https://ros1cancer.com/

Molecular test rates are not acceptable in Germany

Nicht-Plattenepithel-Karzinom	HJ1 2016 (n=157)	HJ2 2016 (n=249)	HJ1 2017 (n=309)	HJ2 2017 (n=492)	HJ1 2018 (n=525)	Gesamt (n=1732)
Auf DrLTs getestet bei Erstlinie						
Yes	141 (89.8%)	232 (93.2%)	290 (93.9%)	464 (94.3%)	504 (96.0%)	1631 (94.2%)
DrLTs tested at 1st-line						
EGFR	117 (74.5%)	197 (79.1%)	233 (75.4%)	372 (75.6%)	396 (75.4%)	1315 (75.9%)
ROS-1	84 (53.5%)	141 (56.6%)	190 (61.5%)	333 (67.7%)	338 (64.4%)	1086 (62.7%)
PD-L1	31 (19.7%)	70 (28.1%)	162 (52.4%)	349 (70.9%)	391 (74.5%)	1003 (57.9%)
ALK	115 (73.2%)	183 (73.5%)	226 (73.1%)	369 (75.0%)	386 (73.5%)	1279 (73.8%)
BRAF	47 (29.9%)	74 (29.7%)	115 (37.2%)	258 (52.4%)	283 (53.9%)	777 (44.9%)

F Griesinger, AIO Herbstkongress 2018

Challenges

- Implementation of centralized high-end molecular multiplex (NGS-based) diagnostics in research-driven cancer centers
- Establishment of regional networks to enable access of all patients with lung cancer
- State-of-the-art, pharma-independent counseling regarding therapeutic consequences of molecular diagnostics
- Rapid innovation transfer (from bench to bedside)
- Evaluation of personalized therapy: data ownership of the patient

Approaches

- Centralized NGS-testing in (national) Network Genomic Medicine containing a clinical trial program with focus on early phase trials → proof of principle for implementation of personalized care

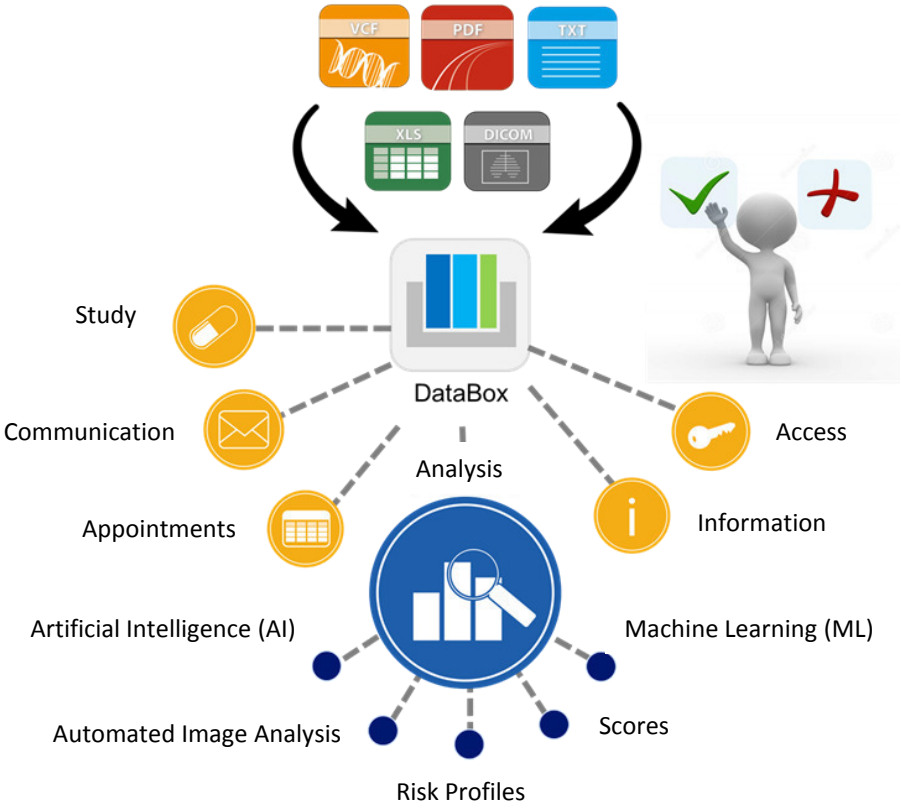
Network Genomic Medicine Lung Cancer

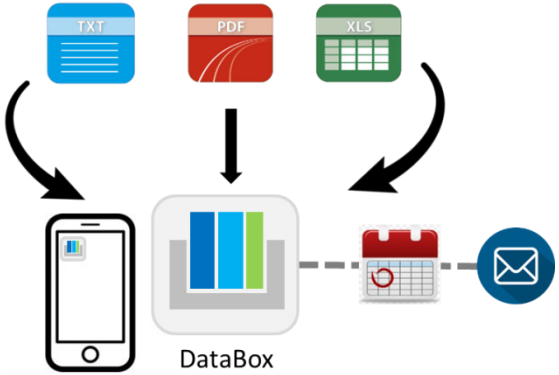
nNGM | National Network Genomic Medicine Lung Cancer

- Improving the availability of data for research through patient empowerment over their data (establishing a patient-centered health data platform) → integration of innovative big-data analysis concepts and artificial intelligence in the platform possible if agreed by individual patient

DataBox

DataBox – patient-centered health platform





Providing patient data in **one central database**

- Available
- Structured
- Functional
- Complete

Patient-empowered data

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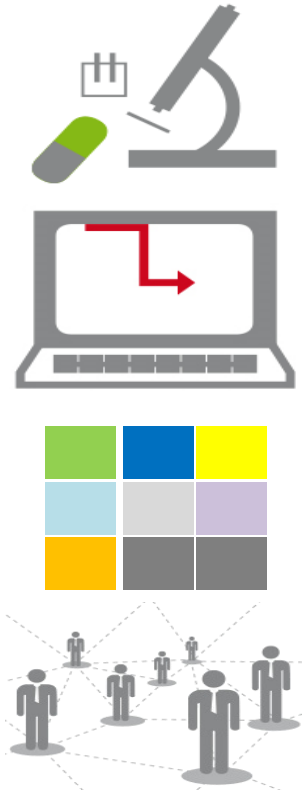
Personalized oncology

- Must **RECONSIDER** old and new approaches
- Provides great **OPPORTUNITIES** for the future
- Needs **INTELLIGENT** data
- Is a **TEAM ACHIEVEMENT**
- Is based on **PATIENT EMPOWERMENT**
- Needs a **LEARNING** (evidence-generating) **SYSTEM**



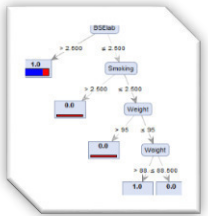
Genomic Data Analysis

High Throughput Genomic Data*

Data Lake

Machine Learning

Predictive Model



Several Machine Learning Use Cases

Diagnose cancer types	•Automated and fast classification •Insight in discriminative features
Predict Tumor Board (TB) treatment decisions	•Reduced TB effort from hrs to min •Deployable where TB unavailable
Predict treatment outcomes	• Treatment success estimation • Best treatment recommend.

Challenges

Dimensionality:
many more variables than patients

Missing data:
genomic studies regularly report missing data

Rarity:
some cancer types very rare

Computat. issues:
high-performance computing HW required

* Leung et al. Machine Learning in Genomic Medicine, Proc. of the IEEE, Vol. 104, No. 1, pp. 176-197, 2016

Exempl. Use-Case: Cancer Classification

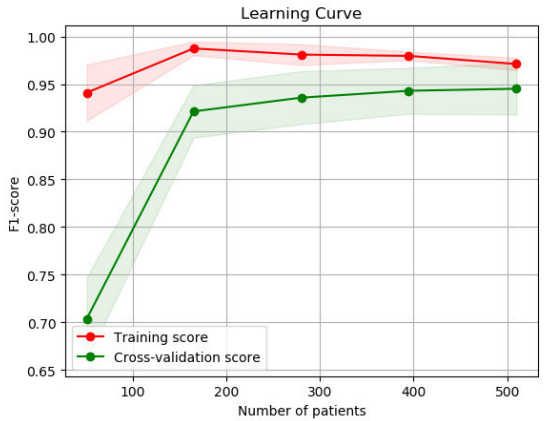
Goal: Can we classify between five cancer types using public gene expression cancer RNA-Seq data*?

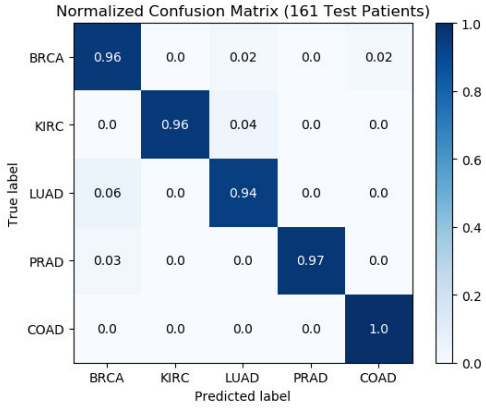
20531!!! features

801 patients

Pat./Feat.	Gene_0	Gene_1	…	Gene_20531	Cancer_type
Pat_1	3.2	1.3	…	4.2	**BRCA**
Pat_2	1.7	2.8	…	3.4	**KIRC**
…	…	…	…	…	**…**
Pat_801	4.3	1.25	…	3.1	**LUAD**

Legend
BRCA: Breast invasive carcinoma
KIRC: Kidney renal clear cell carcinoma
LUAD: Lung adenocarcinoma
PRAD: Prostate adenocarcinoma
COAD: Colon adenocarcinoma





Machine Learning Pipeline
Division / Stratification
Treating missing values
Normalization
Feature extraction
Feature selection
Hyperparameter optimization
Class-weighted modeling
Performance evaluation

Thank you!

Thanks to

the members of the DataBox team at DKFZ (German Cancer Research Center), Siemens Healthineers and SAP

the members of the (n)NGM team for their support in the clinical context and for providing some slides for this presentation

Network Genomic Medicine Lung Cancer

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