



Network  
Genomic Medicine  
Lung Cancer

# **The Network Genomic Medicine (NGM) Lung Cancer**

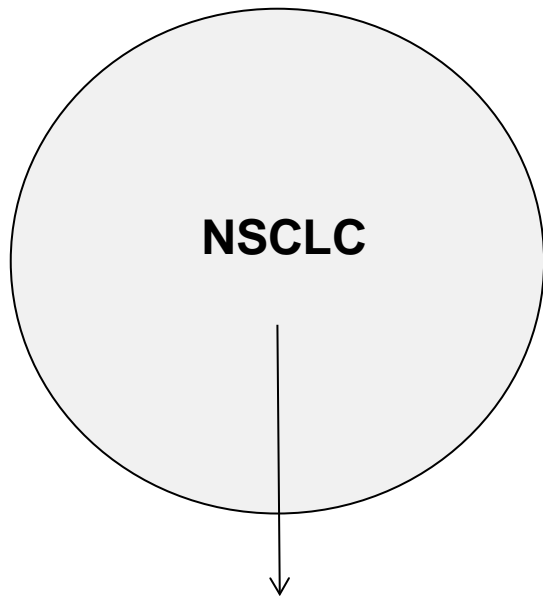
## **- Introduction**

Jürgen Wolf, Cologne - Medical Oncologist

Center for Integrated Oncology, University Hospital of Cologne

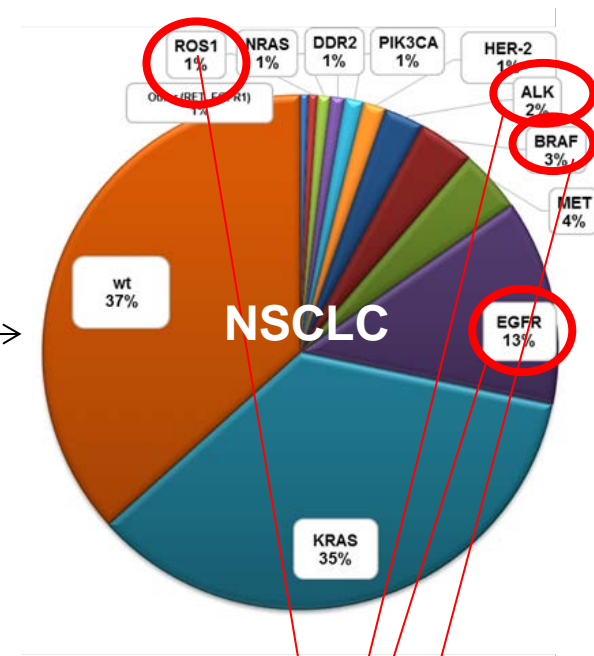
# Systemic cancer therapy turns into personalized therapy: example non-small cell lung cancer (NSCLC)

10 years ago:  
chemotherapy  
in unselected patients



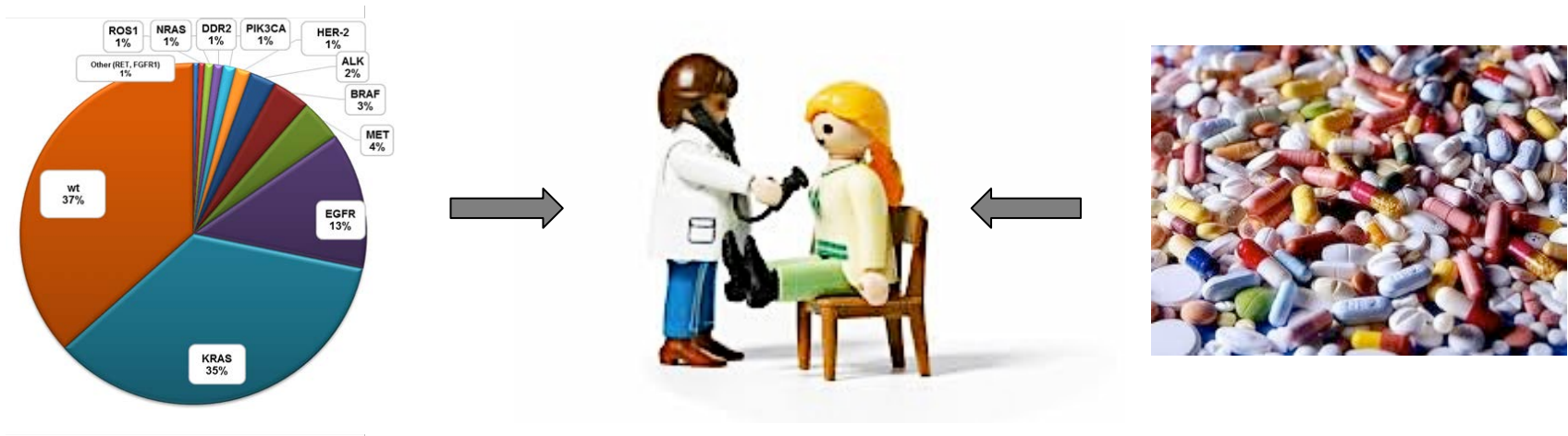
Response Rate: 20-30%  
Med. Survival: 1 year

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



Response Rates: 60 – 70%  
Med. Survival 5 years and more  
Better tolerability

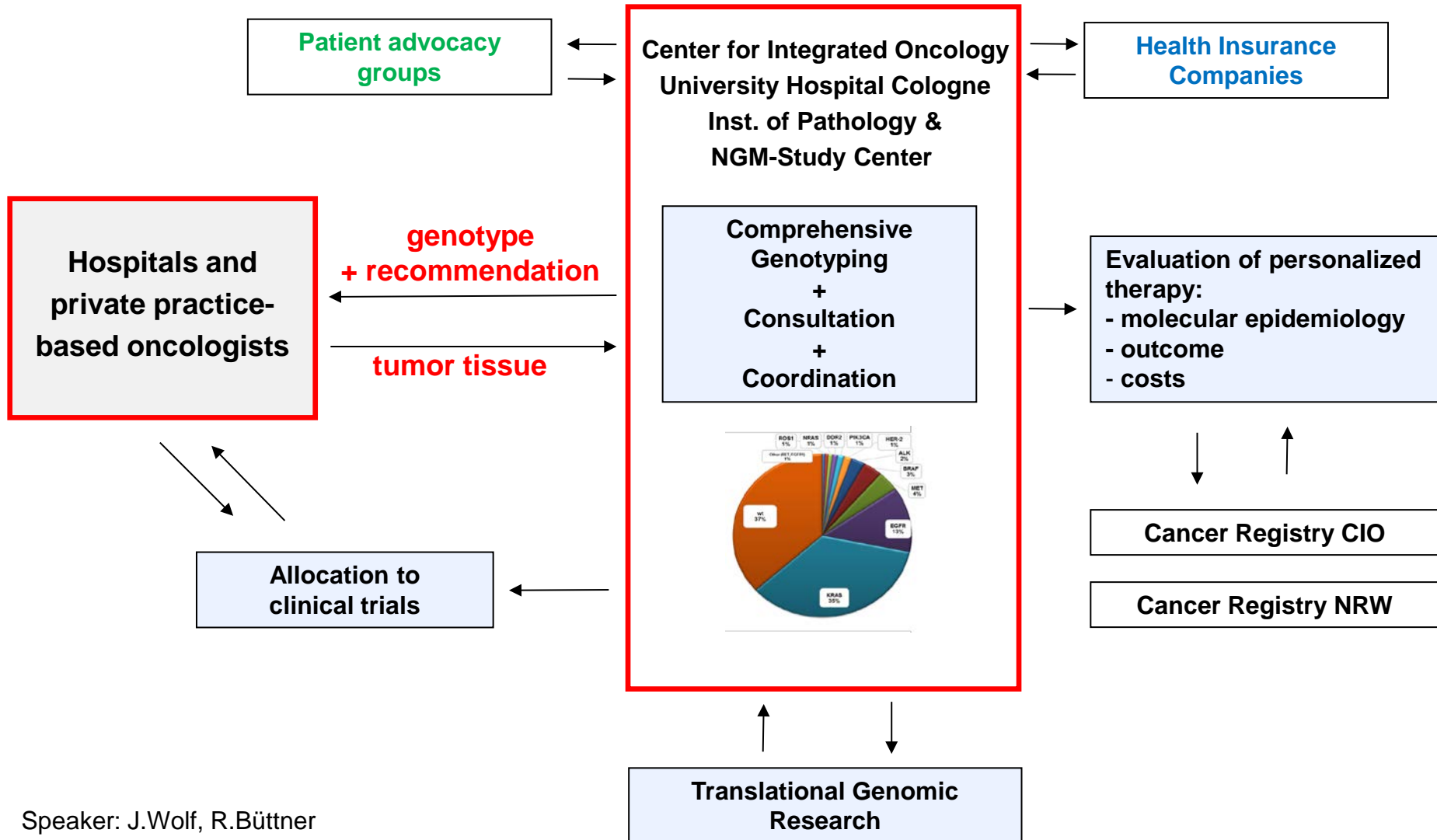
# Challenges for the implementation of personalized cancer care into clinical routine



- Implementation of high-quality **molecular multiplex diagnostics**
- State-of-the-art **consultation** with regard to therapeutic consequences
- Rapid **innovation transfer** (new driver mutations) from the academic centers into broad cancer patient care
- **Evaluation** of post-approval and off-label personalized therapies

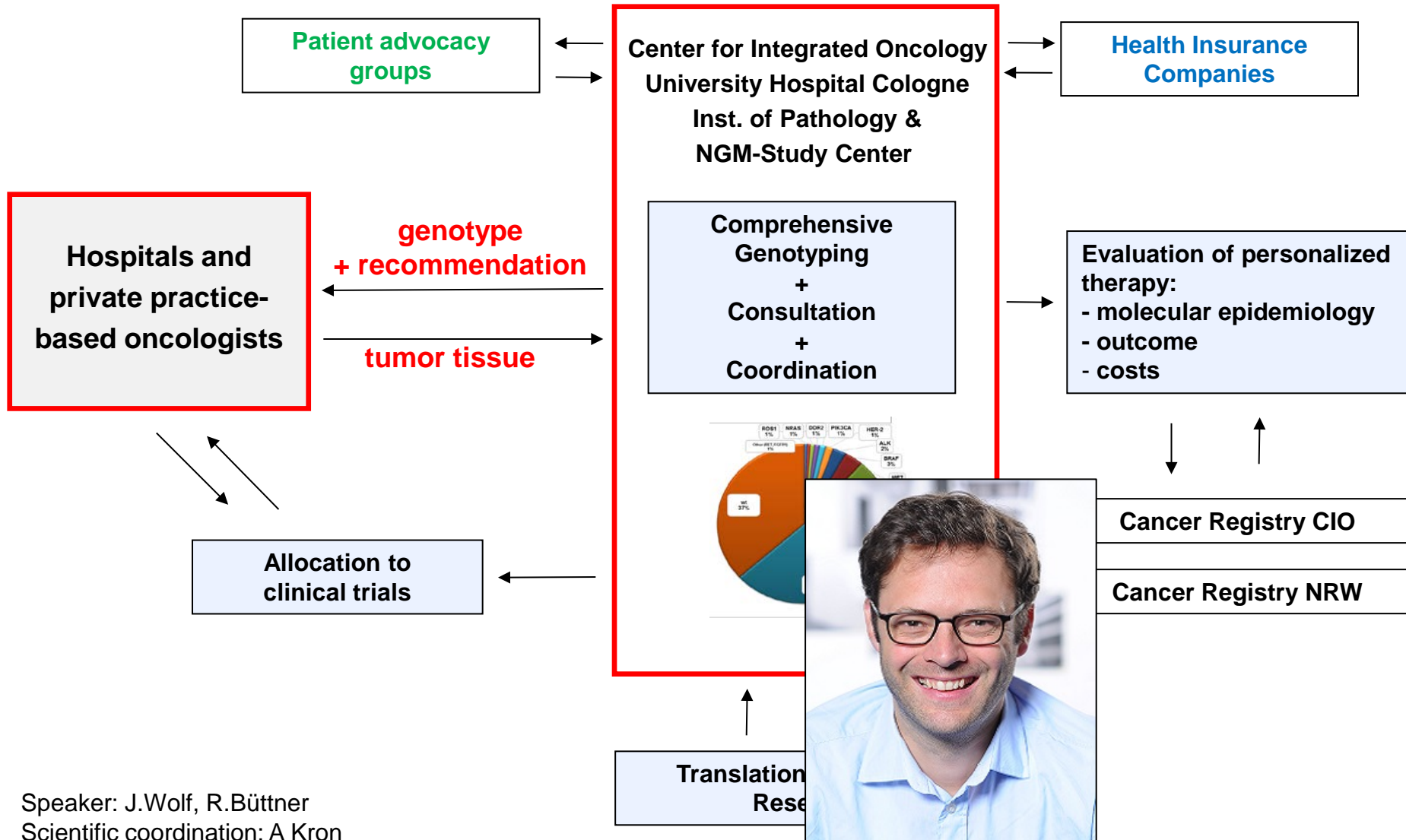
# Network Genomic Medicine:

Founded in 2010 with funding from Ministry for Innovation and Research NRW



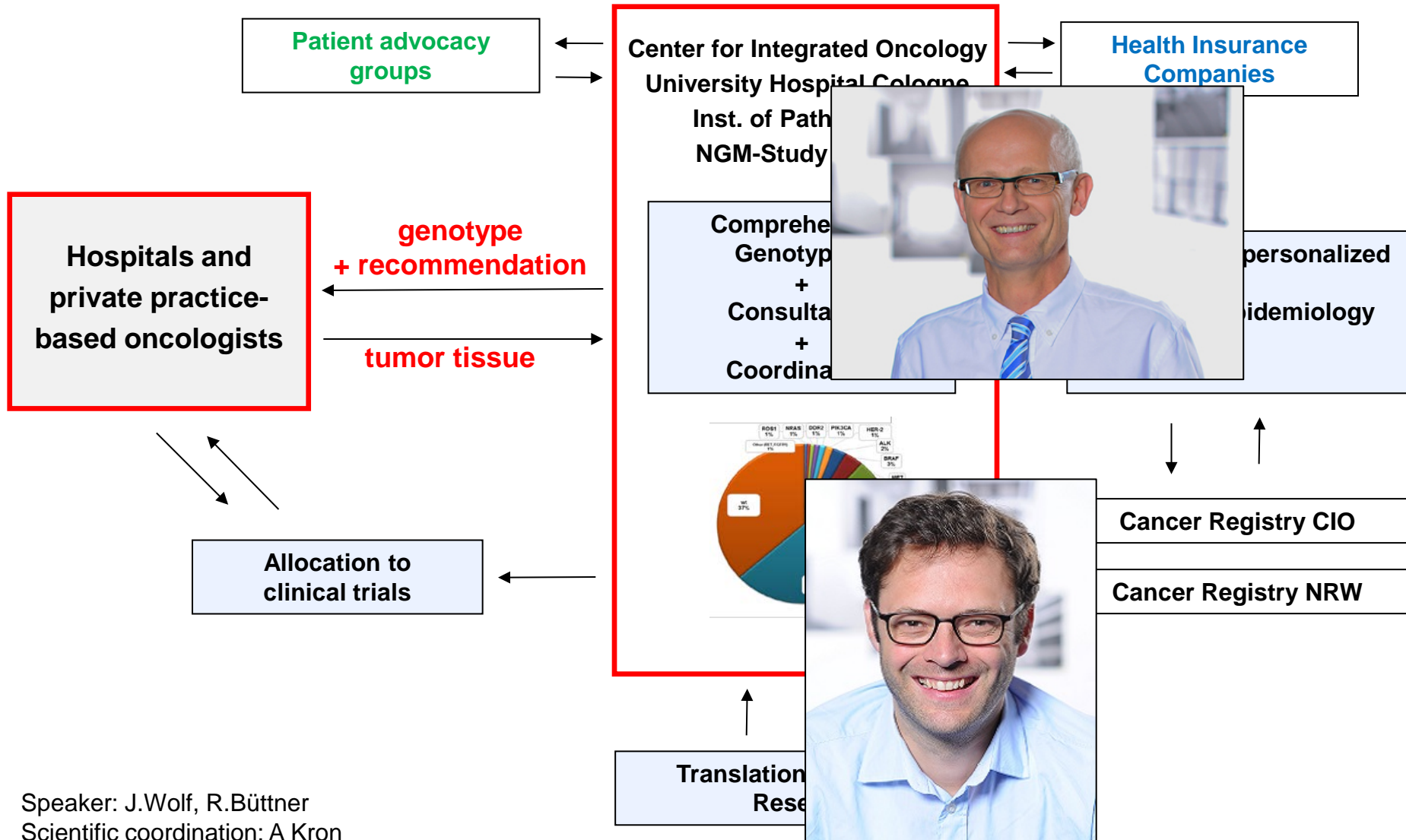
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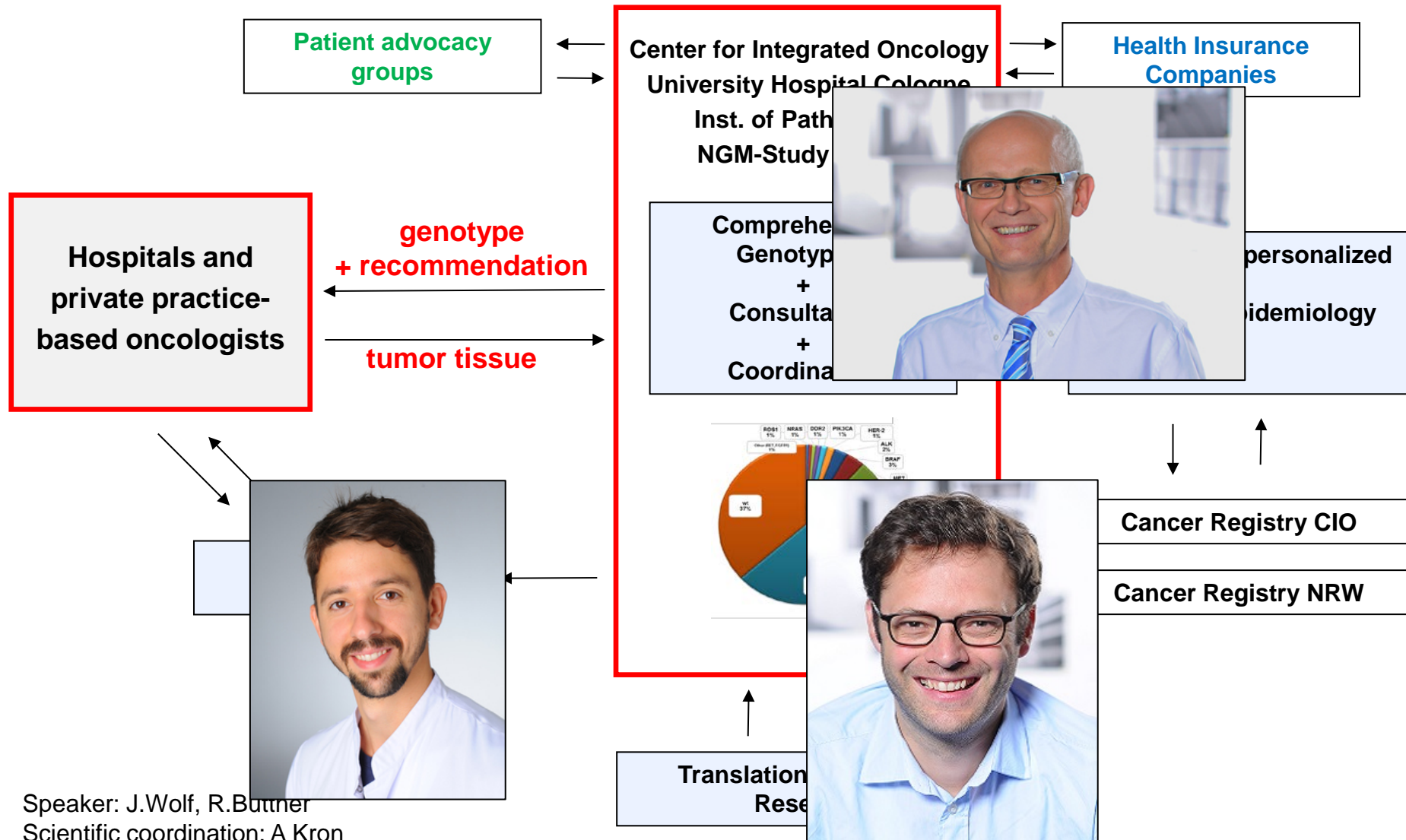
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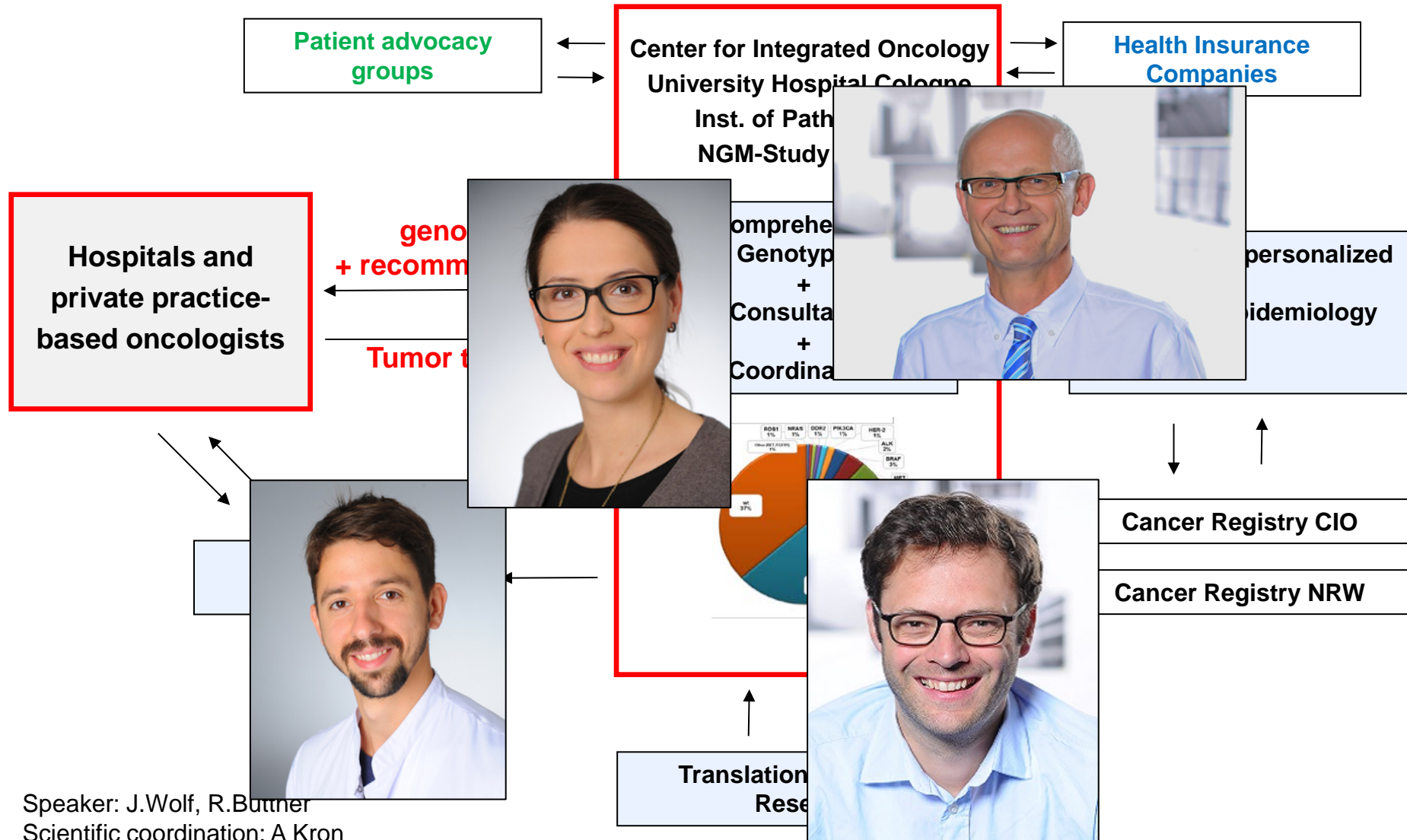
Founded in 2010 with funding from Ministry for Innovation and Research NRW





# Network Genomic Medicine:

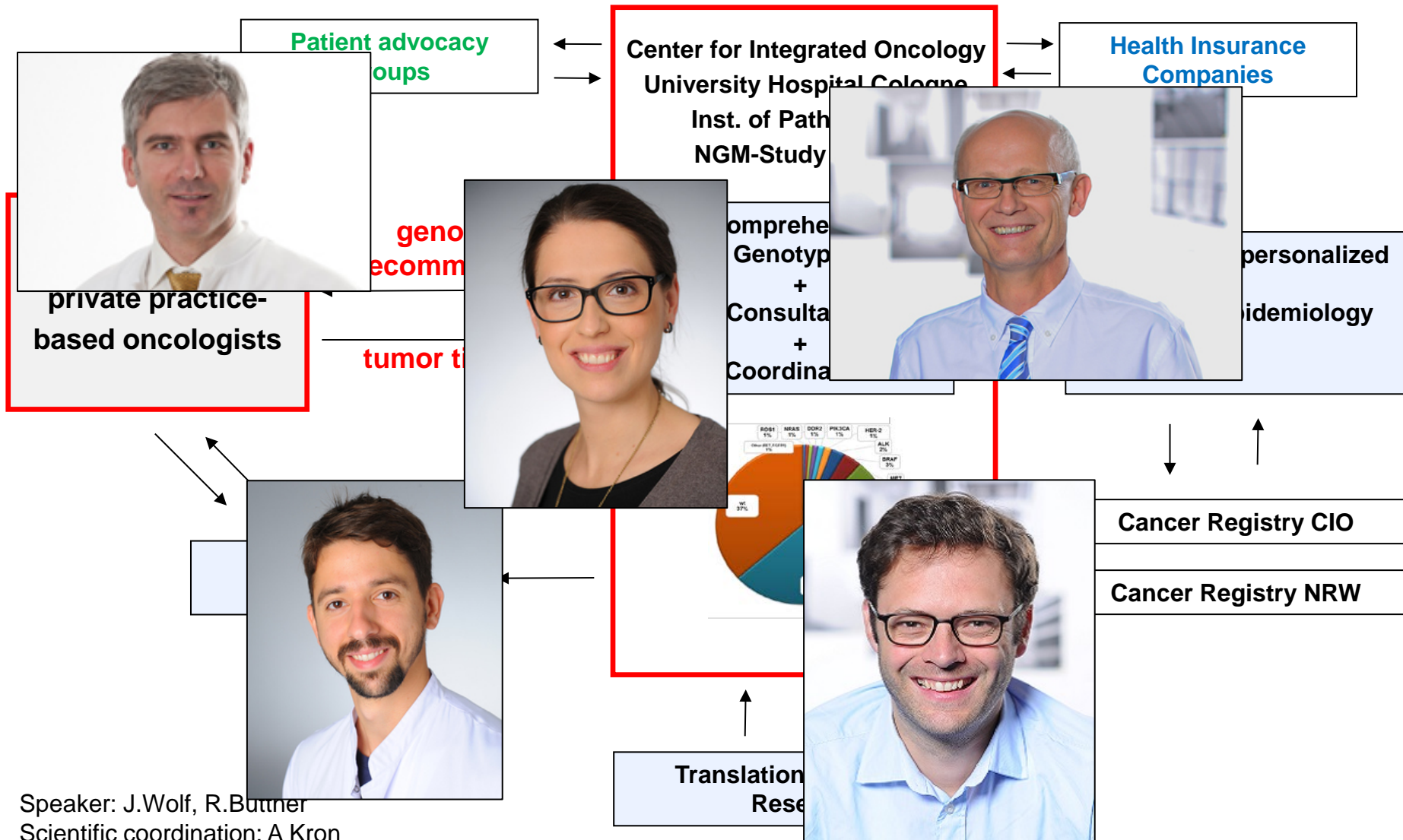
Founded in 2010 with funding from Ministry for Innovation and Research NRW





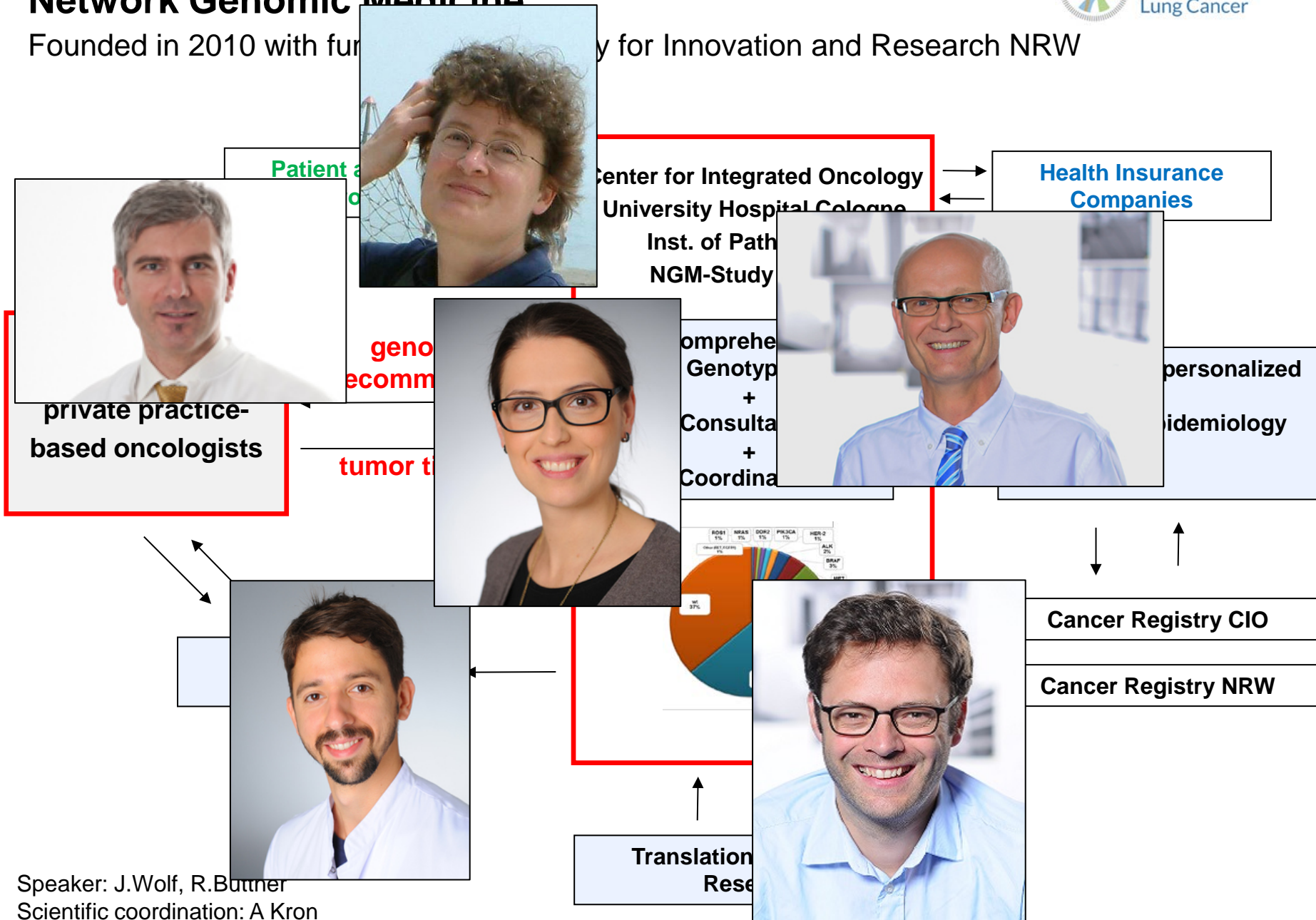
# Network Genomic Medicine:

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# Network Genomic Medicine:

Founded in 2010 with funding from the Ministry for Innovation and Research NRW



Speaker: J.Wolf, R.Buttner  
 Scientific coordination: A Kron

# Network Genomic Medicine:

Founded in 2010 with funding from the Ministry for Innovation and Research NRW



Patient a  
o

Center for Integrated Oncology  
University Hospital Cologne

Inst. of Pathology  
NGM-Study



private practice-  
based oncologists

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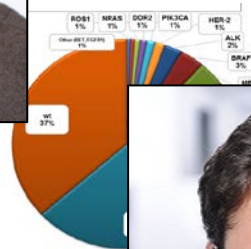
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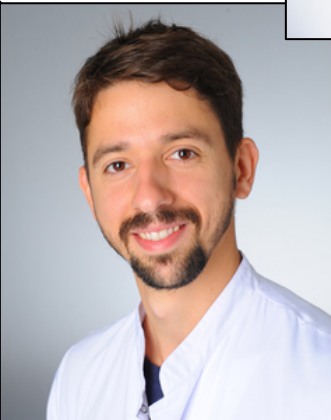


personalized  
epidemiology



Cancer Registry CIO

Cancer Registry NRW



Translation  
Rese



Speaker: J. Wolf, R. Buttner  
Scientific coordination: A. Kron



Network  
Genomic Medicine  
Lung Cancer

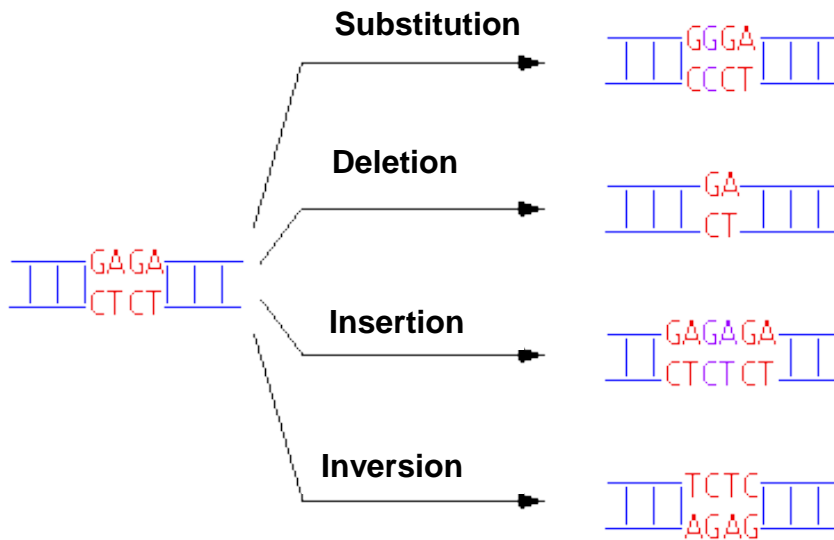
## **The Genomic Approach**

Roman Thomas, Cologne – Genome Researcher

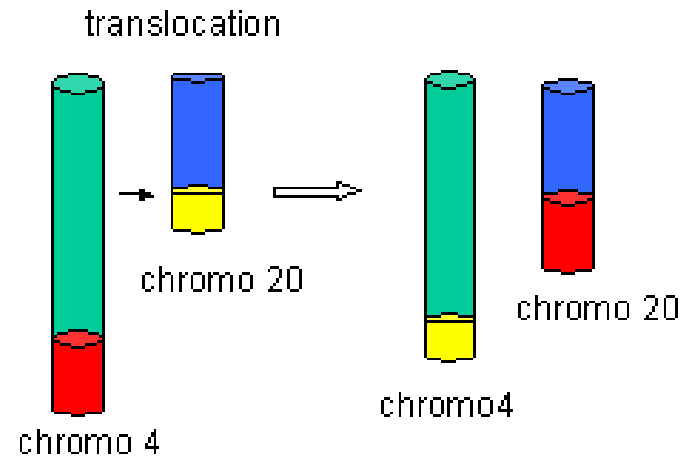
University of Cologne and German Cancer Research Institute (DKFZ)

# Cancer is a disease of the genome

## Subtle sequence alterations



## Complex structural alterations

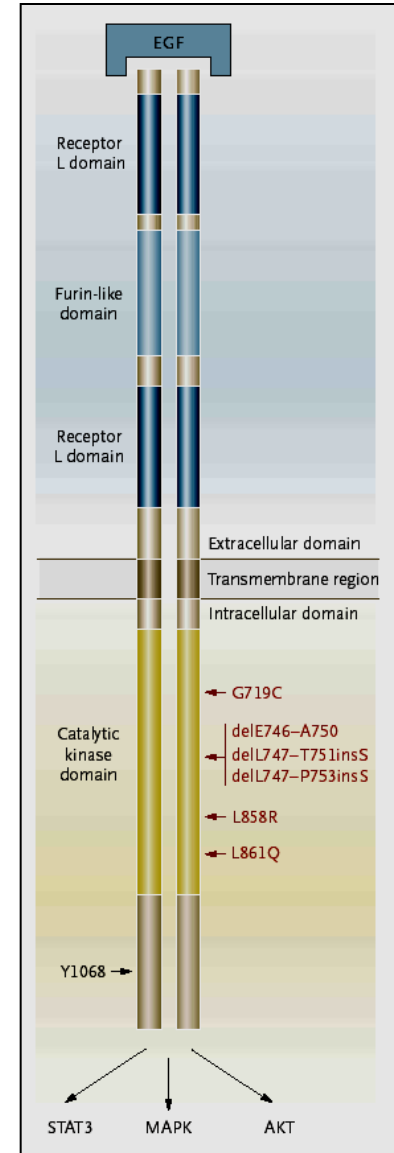


## Chromosomal copy-number alterations



# EGFR mutations in lung cancer

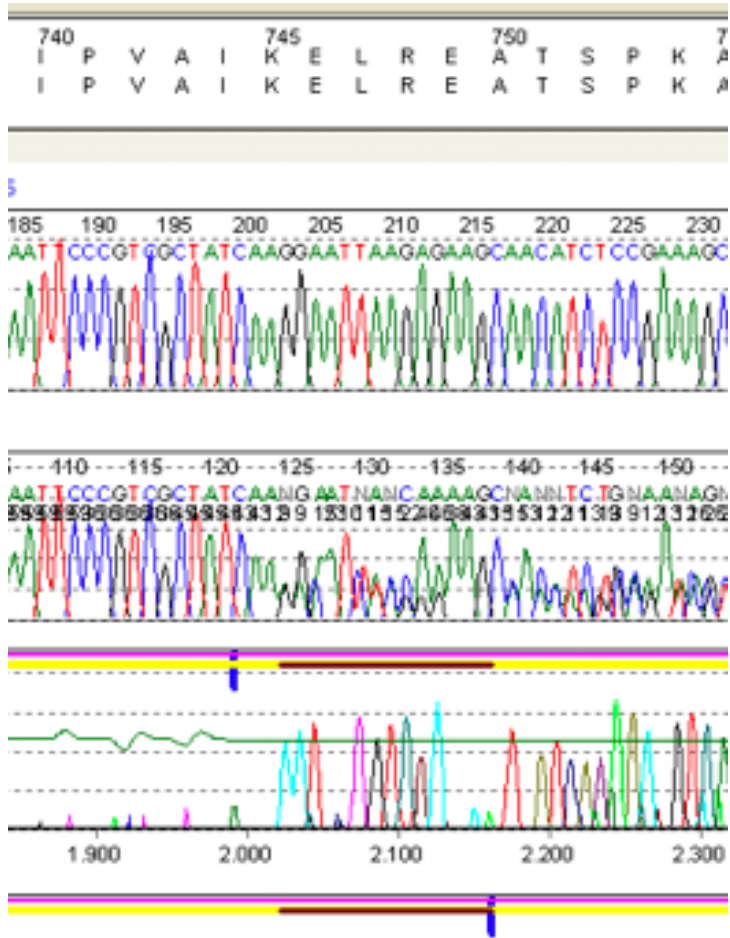
- Mutations in the EGFR kinase domain: 10% of lung cancer
- EGFR mutations associate with response to EGFR Inhibitors Erlotinib und Gefitinib
- (Seminal discoveries made by the Meyerson, Haber and Varmus labs in 2004)



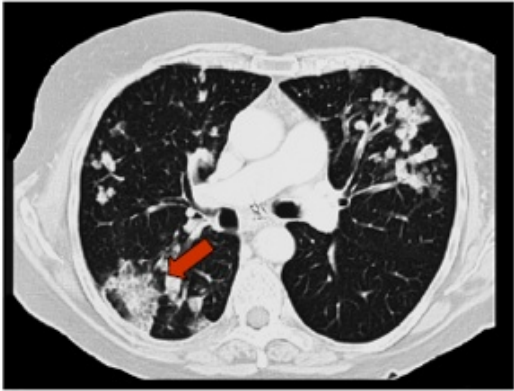


# EGFR mutation and response to EGFR inhibition, the clinical example

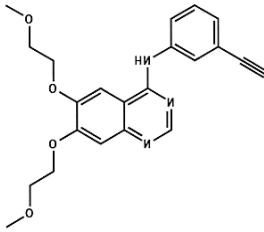
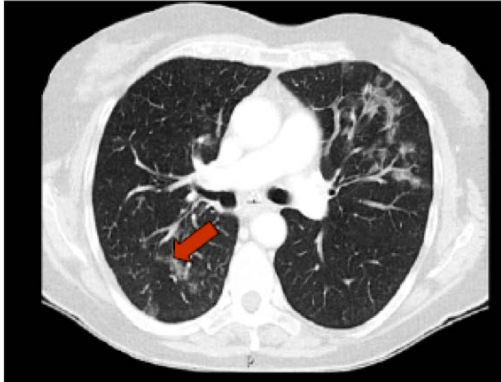
Heterozygous EGFR  
E746\_A750del mutation



Pre-therapy



6 weeks of erlotinib





**The Cancer Genome Atlas**

**EGFR Mutations in Lung Cancer: Correlation with Clinical Response to Gefitinib Therapy**

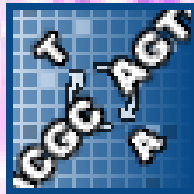
**Human Breast and Colorectal Cancer Kinase Mutations**

**Patterns of somatic mutation in human cancer genomes**

Tobias-Sjöblom<sup>1,2\*</sup>, Silin Jones<sup>1,2\*</sup>, Laura D. W...  
 Thomas D. Barber<sup>1,2</sup>, Oriana Mandelker<sup>1,2</sup>,  
 Steve Szabo<sup>1,2</sup>, Phillip Buckhaults<sup>1,2</sup>,  
 Joseph Willis<sup>1,2</sup>, Dawn Dawson<sup>1,2</sup>,  
 Changping Liu<sup>1,2</sup>, Giovanni...  
 Nicholas Papadopoulos<sup>1,2</sup>

Janne<sup>1,2\*</sup>, Jeffrey C. Lee<sup>1,2\*</sup>,  
 Corey Gabriel<sup>1,2</sup>, Paula Herman<sup>1,2</sup>,  
 Titus J. Boggon<sup>1,2</sup>,  
 Shitaka Fujii<sup>1,2</sup>,  
 ...<sup>1,2,4</sup>

Christopher Greenman<sup>1</sup>, Philip Stephens<sup>1</sup>, Raffaella Smith<sup>1</sup>, Gillian L. Dalgleish<sup>1</sup>, Christopher Hunter<sup>1</sup>,  
 Graham Bignell<sup>1</sup>, Helen Davies<sup>1</sup>, Jon Teague<sup>1</sup>, Adam Butler<sup>1</sup>, Claire Stevens<sup>1</sup>, Sarah Edkins<sup>1</sup>, Sarah O'Meara<sup>1</sup>,  
 Imre Vastrik<sup>2</sup>, Esther E. Schmidt<sup>2</sup>, Tim Avis<sup>1</sup>, Syd Barthorpe<sup>1</sup>, Gurpreet Bhamra<sup>1</sup>, Gemma Buck<sup>1</sup>,  
 Bhudipa Choudhury<sup>1</sup>, Jody Clements<sup>1</sup>, Jennifer Cole<sup>1</sup>, Ed Dicks<sup>1</sup>, Simon Forbes<sup>1</sup>, Kris Gray<sup>1</sup>, Kelly Halliday<sup>1</sup>,  
 Rachel Harrison<sup>1</sup>, Katy Hills<sup>1</sup>, Jon Hinton<sup>1</sup>, Andy Jenkinson<sup>1</sup>, David Jones<sup>1</sup>, Andy Menzies<sup>1</sup>, Tatiana Mironenko<sup>1</sup>,  
 Janet Perry<sup>1</sup>, Keiran Raine<sup>1</sup>, Dave Richardson<sup>1</sup>, Rebecca Shepherd<sup>1</sup>, Alexandra Small<sup>1</sup>, David N. Louis<sup>1</sup>, Peter Goldstraw<sup>1</sup>,  
 Tony Webb<sup>1</sup>, Sofie West<sup>1</sup>, Sara Widaa<sup>1</sup>, Andy Yates<sup>1</sup>, Daniel P. Cahill<sup>1</sup>, Barbara L. Weber<sup>1</sup>, Yoke-Eng Chiew<sup>1</sup>,  
 Andrew G. Nicholson<sup>1</sup>, Francis Brasseur<sup>1</sup>, Leendert Looijenga<sup>1</sup>, Peter Campbell<sup>1</sup>, Douglas F. Easton<sup>11</sup>,  
 Anna deFazio<sup>1</sup>, Mel F. Greaves<sup>1</sup>, Anthony R. Green<sup>10</sup>, Peter Campbell<sup>1</sup>, Barbara L. Weber<sup>1</sup>, Yoke-Eng Chiew<sup>1</sup>,  
 Georgia Chenevix-Trench<sup>12</sup>, Min-Han Tan<sup>13</sup>, Sok Kean Khoo<sup>13</sup>, Bin Tean Teh<sup>13</sup>, Siu Tsan Yuen<sup>14</sup>, Suet Yi Leung<sup>14</sup>,  
 Richard Wooster<sup>1</sup>, P. Andrew Futreal<sup>1</sup> & Michael R. Stratton<sup>1,9</sup>



THE CANCER GENOME ATLAS 



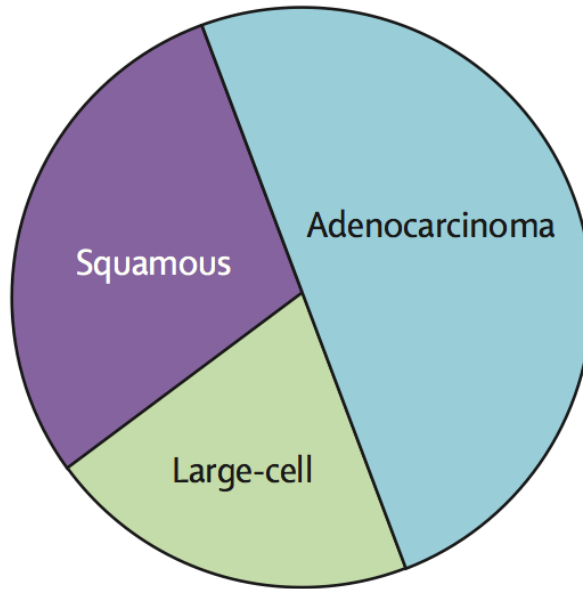
Human Genome  
 Baylor College of Medicine

AIO meeting 2007

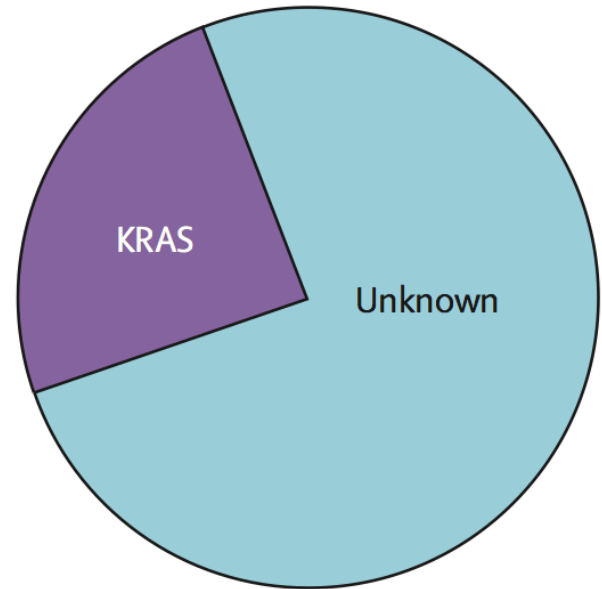
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 GATGGCGGTTACCAAGTCTGGAGTCAATGGCGGTTACCAAGTCTGGAGTCAAT  
 TACCAAGTCTGGCGTTACCAAGTCTGGAGTCAATGGCGGTTACCAAGTCTGGAGTCAAT  
 TGGCGGTTACCAAGTCTGGAGTCAATGGCGGTTACCAAGTCTGGAGTCAAT

# The genomic evolution of lung adenocarcinoma

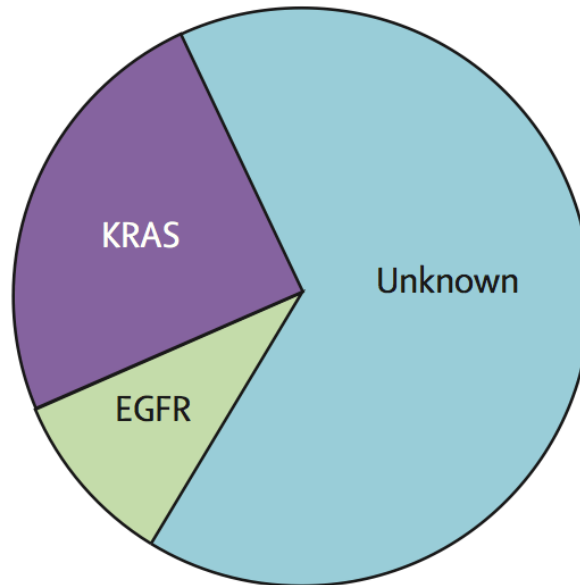
Traditional view



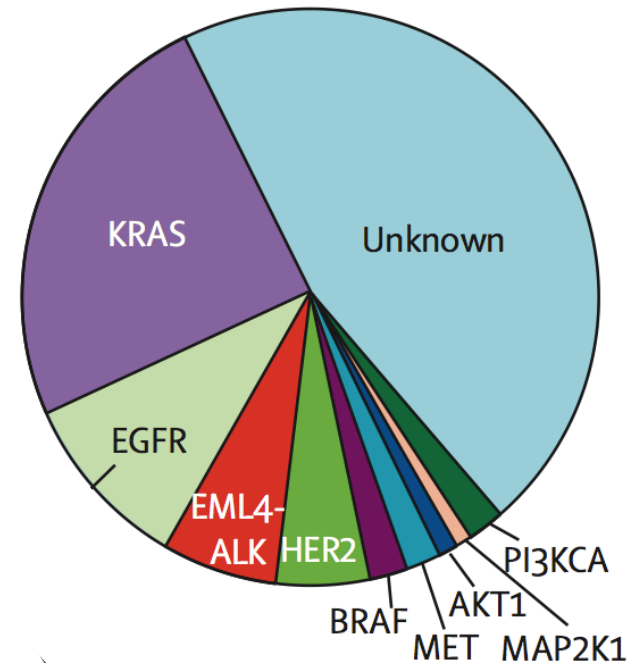
1987



2004

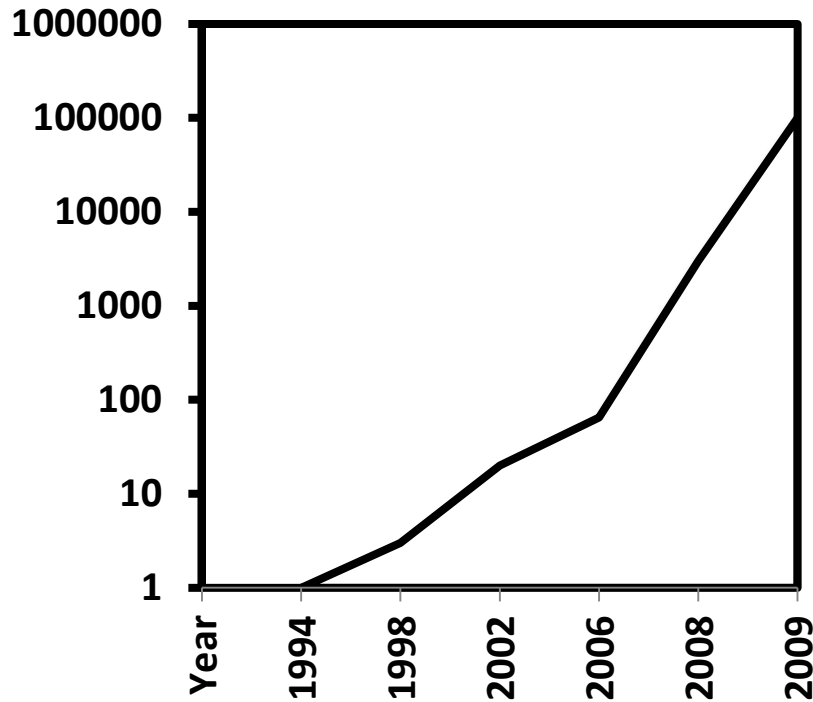


2009

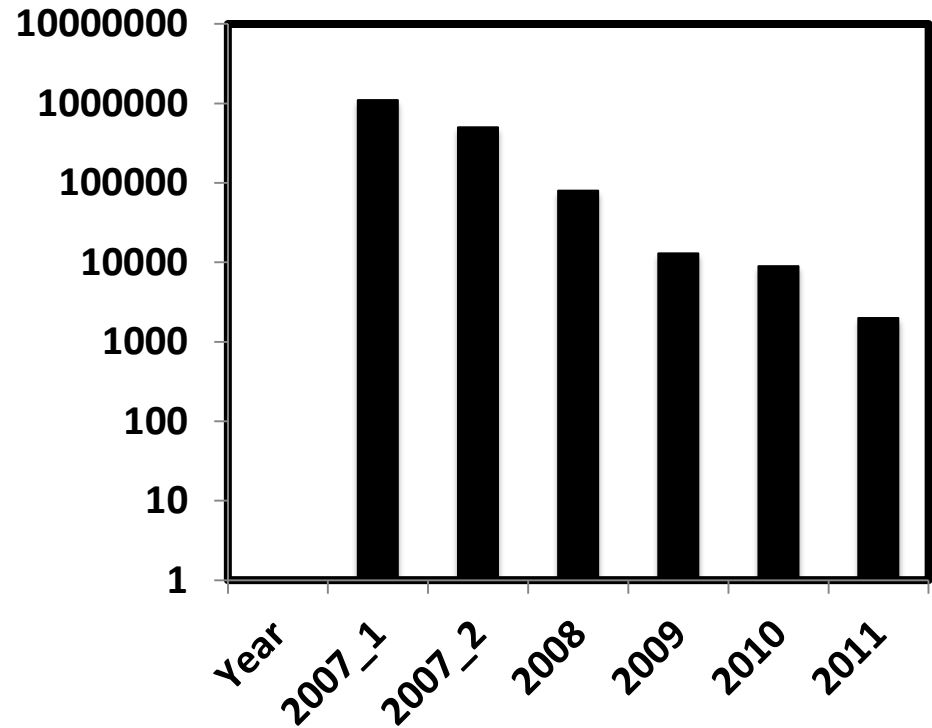


# Development of sequencing output and costs

## Gigabases

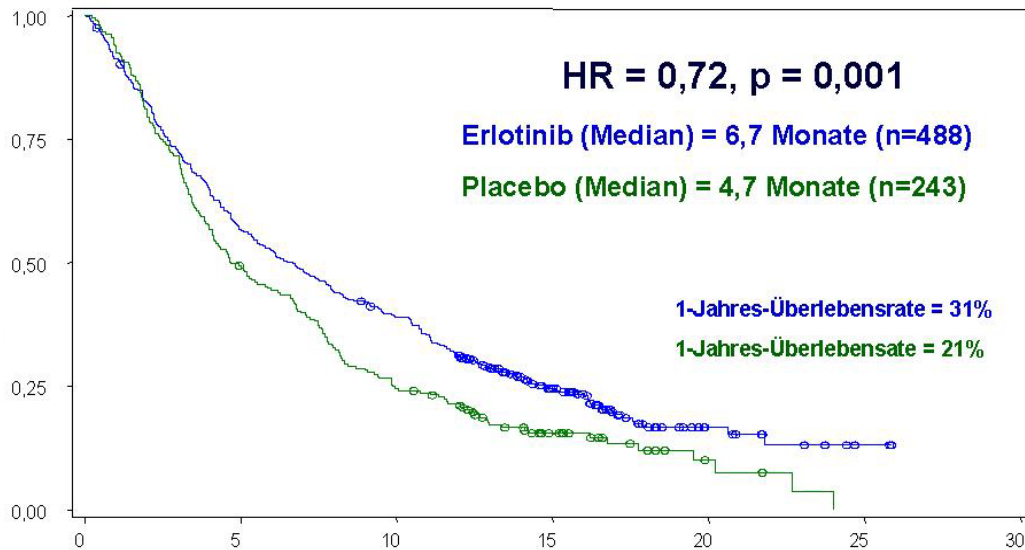


## Costs



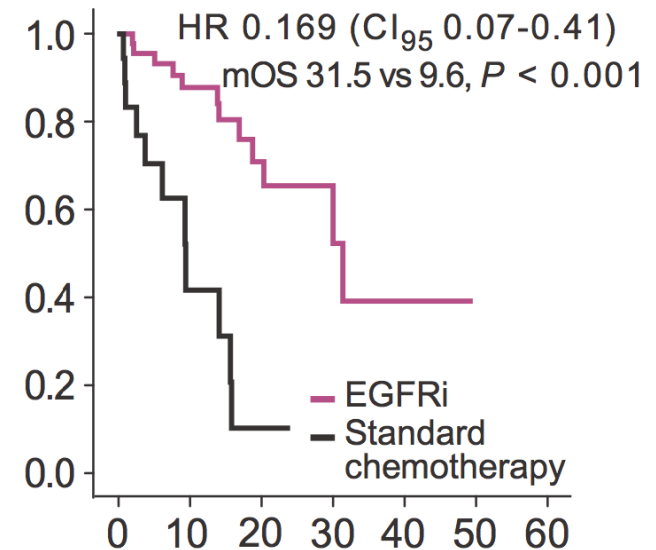
# Genomic information: a new disruptive standard of personalized oncology

## EGFR inhibitor, no selection



Survival chemo  
Survival EGFRi, no selection  
Survival EGFRi, selection

## EGFR inhibitor, selection



app. 1y  
app. 1y  
app. 3y

# The role of genomics in clinical oncology

- First single breakthrough technology to change cancer patients' lives
- New opportunities for discovery and...
- ...diagnostics alike





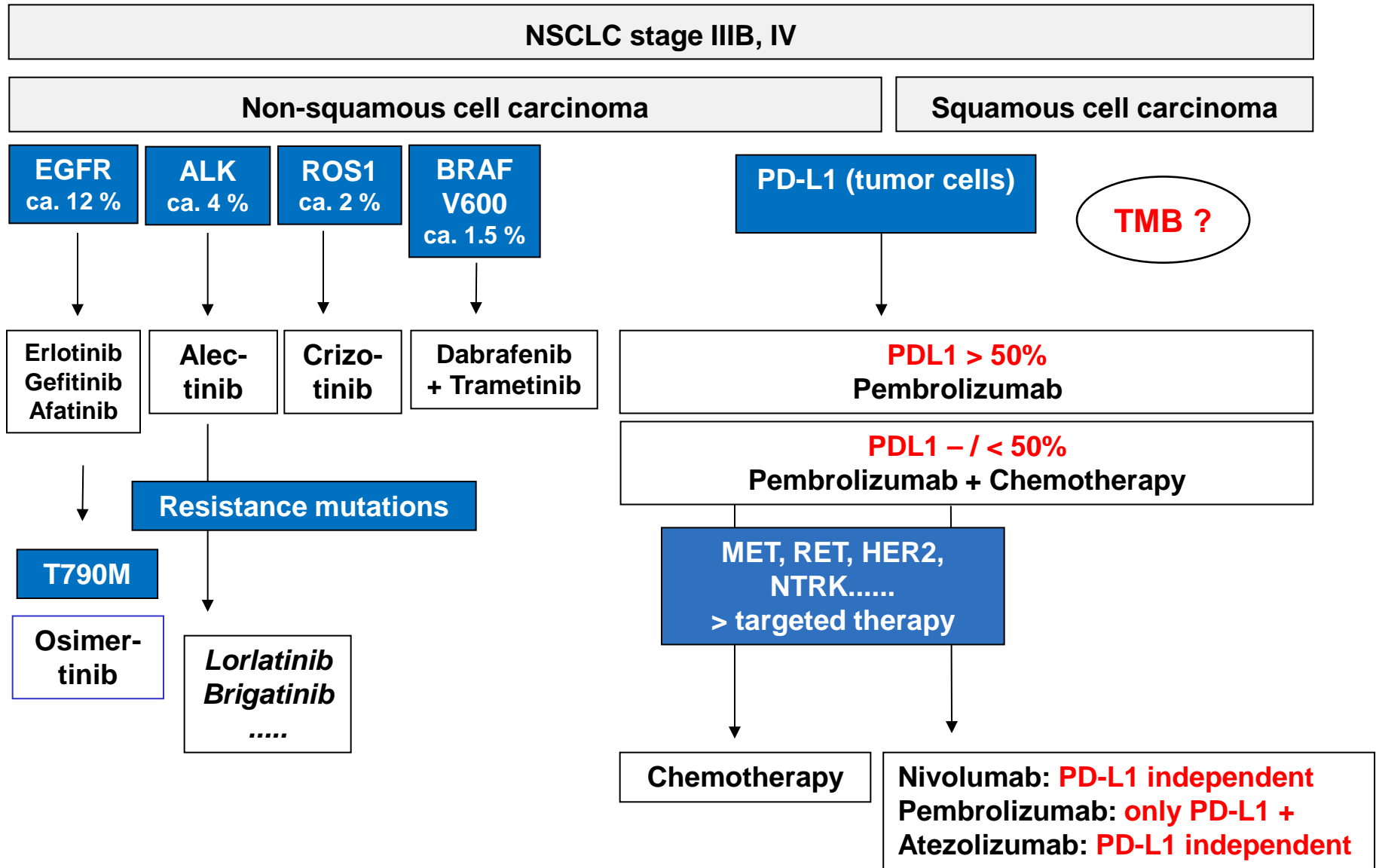
Network  
Genomic Medicine  
Lung Cancer

## **High-end Molecular Diagnostics**

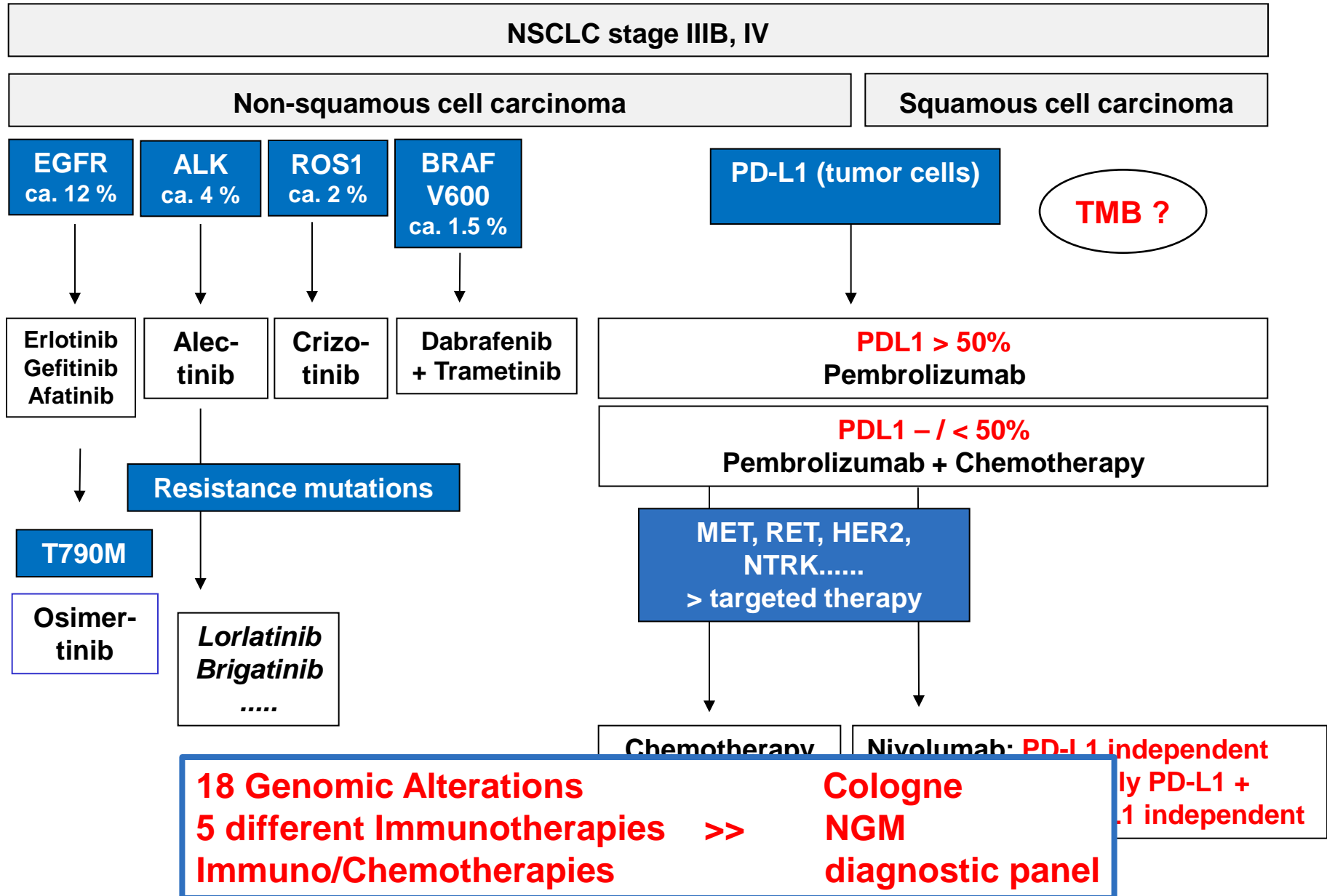
Reinhard Büttner, Cologne – Pathologist

Center for Integrated Oncology, University Hospital of Cologne

# Systemic therapy of NSCLC is increasingly guided by biomarkers



# Systemic therapy of NSCLC is increasingly guided by biomarkers



# Network Genomic Medicine: Integrating High-end Molecular Diagnostics and Oncological Expertises

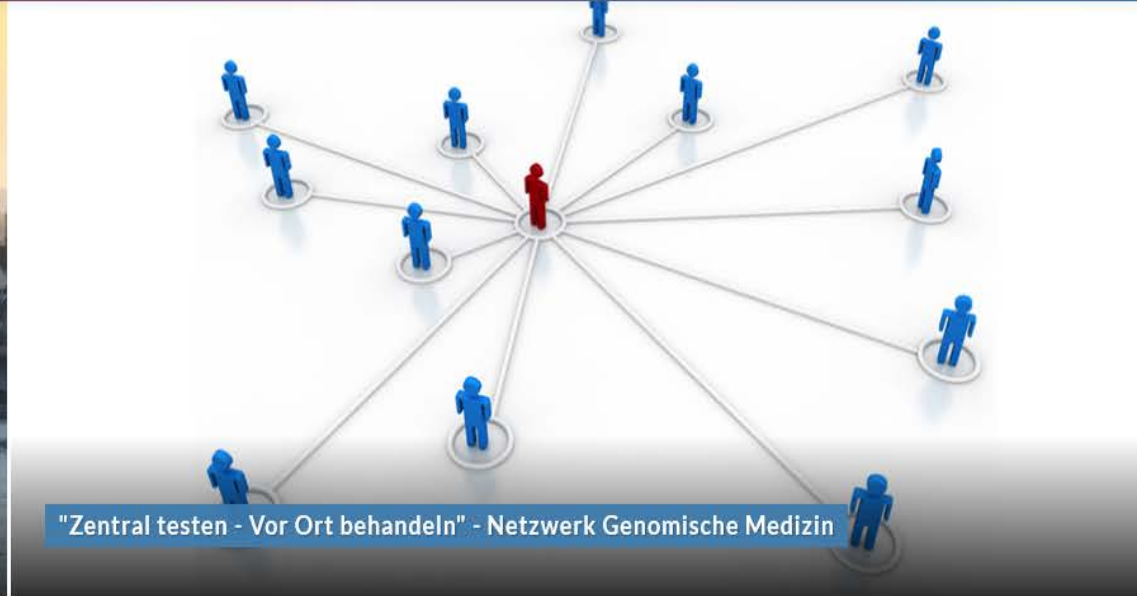


Netzwerk  
Genomische Medizin  
Lungenkrebs

Ärzte Patienten Über uns LCGC EN



NGM stellt neue Daten vor



"Zentral testen - Vor Ort behandeln" - Netzwerk Genomische Medizin

## Noch kein Mitglied?



Als Kooperationspartner des Integrierten Versorgungsvertrages haben Sie die Möglichkeit, kostenlos die molekulare Diagnostik für Ihre Patienten bei uns anzufordern.

[MITGLIED WERDEN](#)

## Mitglieder in Ihrer Nähe



Im NGM arbeiten Krankenhäuser und Facharztpraxen interdisziplinärer Fachrichtungen sektorübergreifend zusammen. Finden Sie den Netzwerkkooperationspartner in Ihrer Nähe.

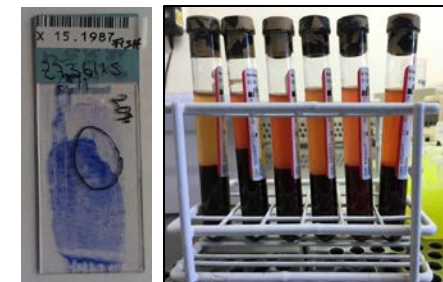
[MITGLIEDER FINDEN](#)

## Diagnostik anfordern



Sie wollen die Diagnostik für Ihre Patienten anfordern? Faxen Sie uns einfach den Anforderungsschein inkl. Patienteneinwilligung zu: 0221-478-3531

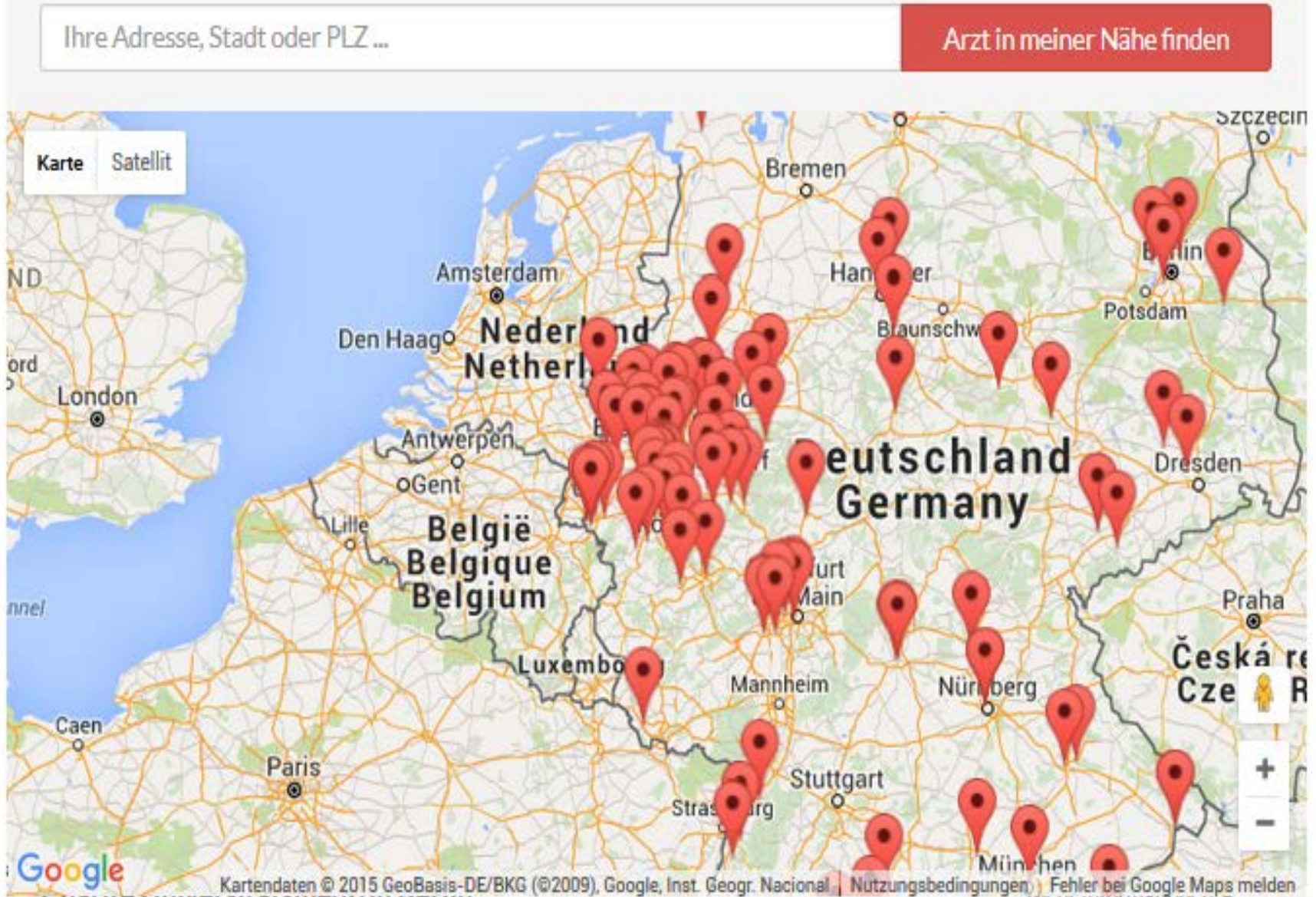
[ANFORDERUNGSSCHEIN](#)



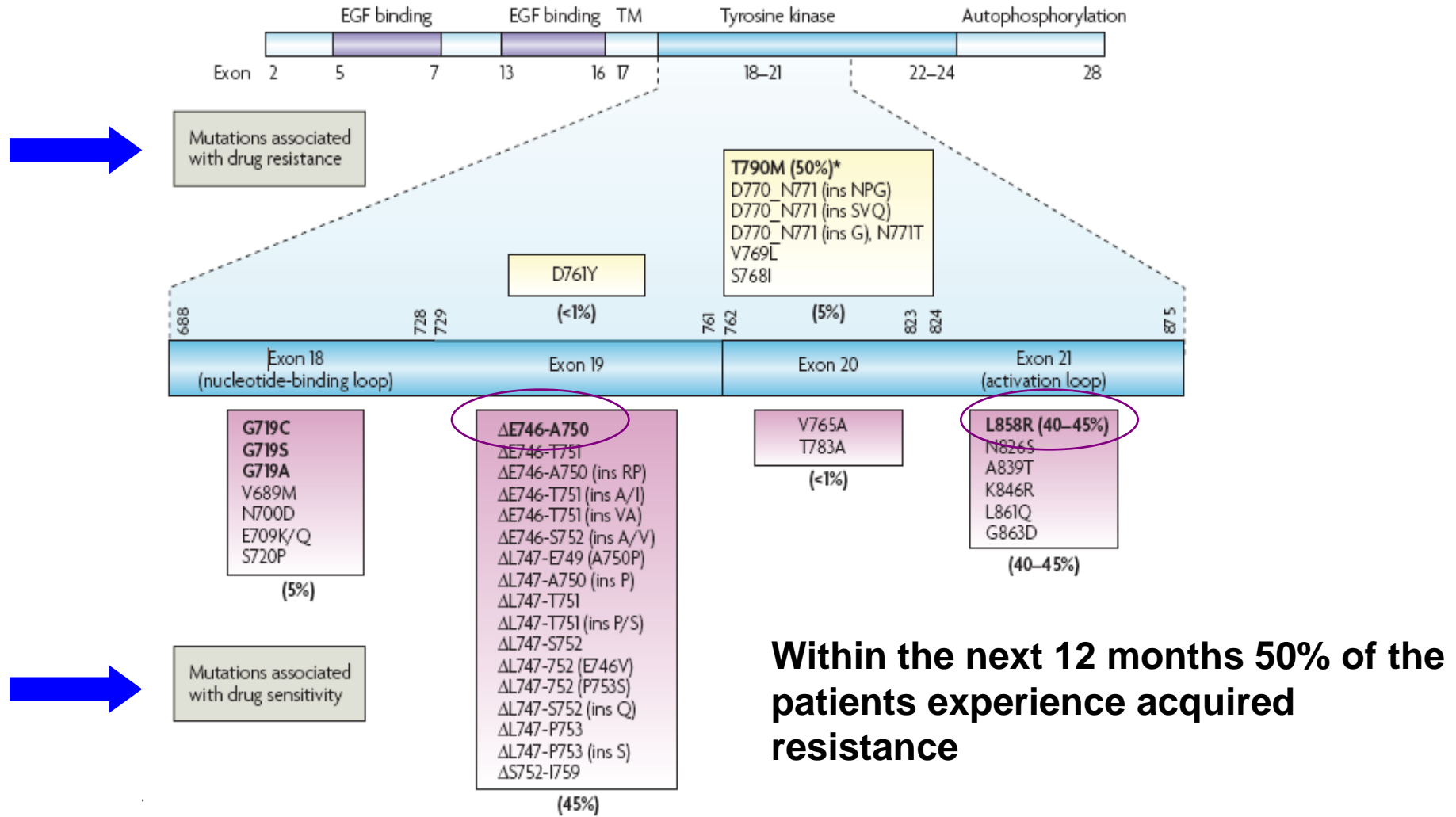


# Less than 10% diagnostic failure rate Treatment at partnering sites

2012: n ~ 500    2016: n ~ 5,000 cases



# EGFR mutation detected in NSCLC

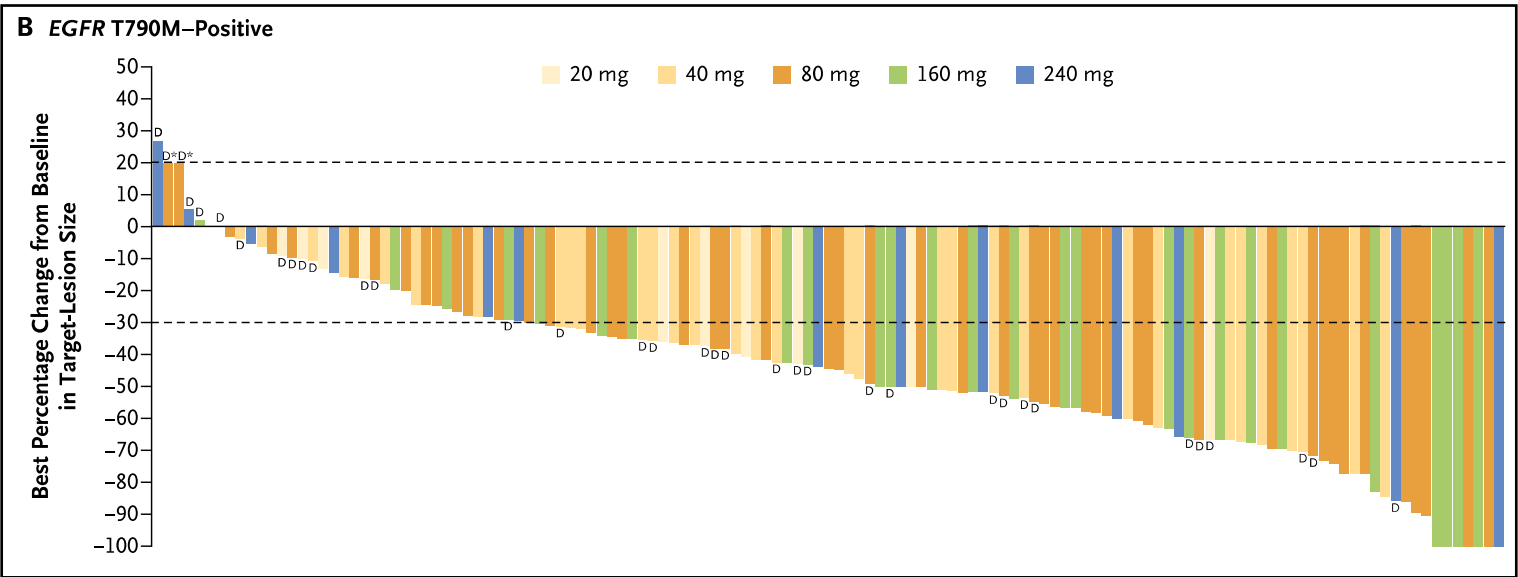


**Within the next 12 months 50% of the patients experience acquired resistance**

**~ 60% T790M mutation in EGFR ex20**

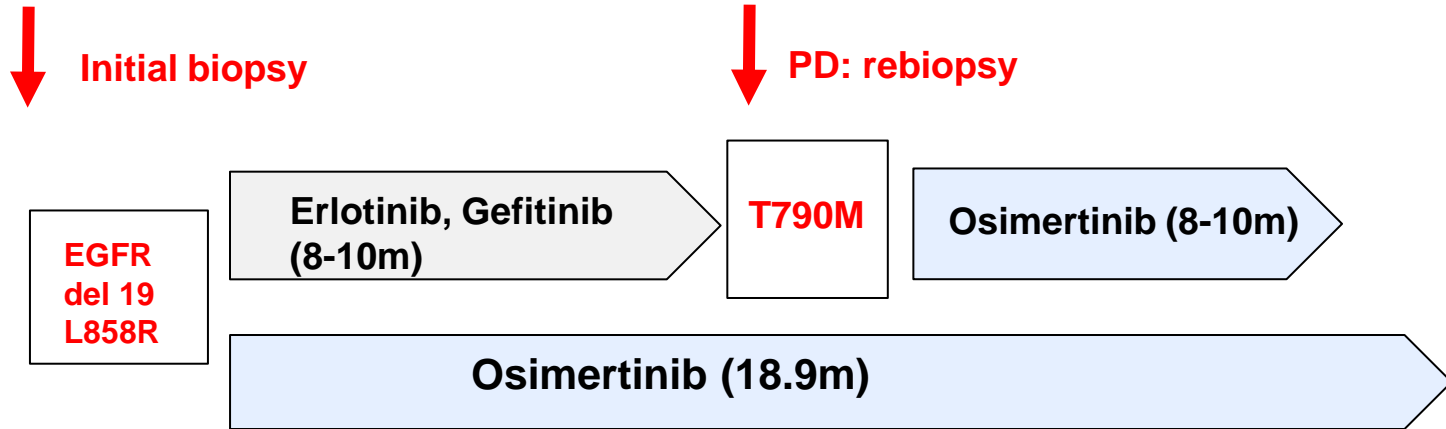


# Clinical efficacy of 3<sup>rd</sup> gen. EGFR inhibitors

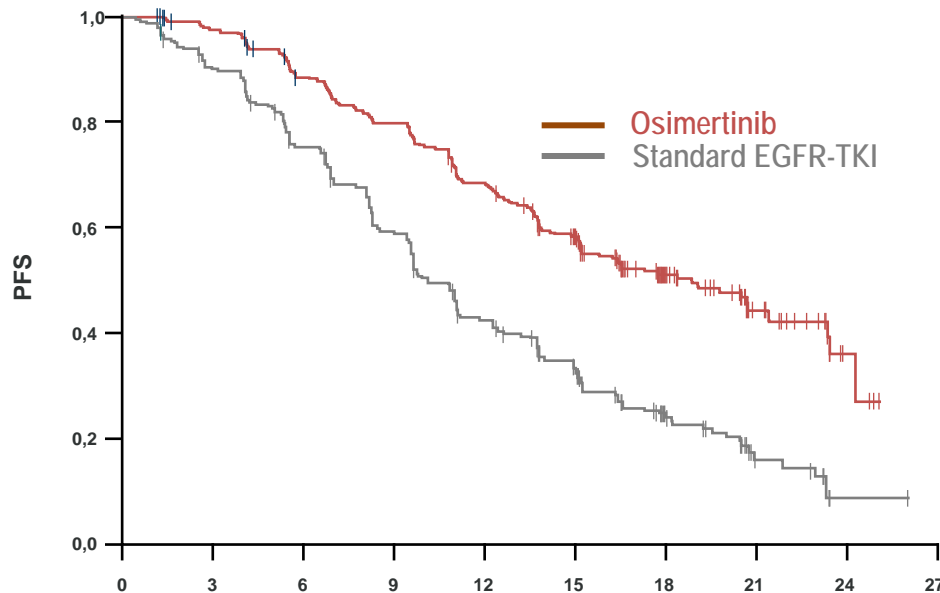


**Phase I (Aura): mPFS 9.6 m**  
**ORR: 61%**  
**DCR: 95%**

# 3<sup>rd</sup> gen. EGFR-TKI as 1<sup>st</sup> line therapy are superior to 1<sup>st</sup> gen. inhibitors



**FLAURA  
Phase III  
Osimertinib  
vs. Standard  
EGFR-TKI**



**Median PFS, months (95%KI)**

**18,9 (15,2; 21,4)**

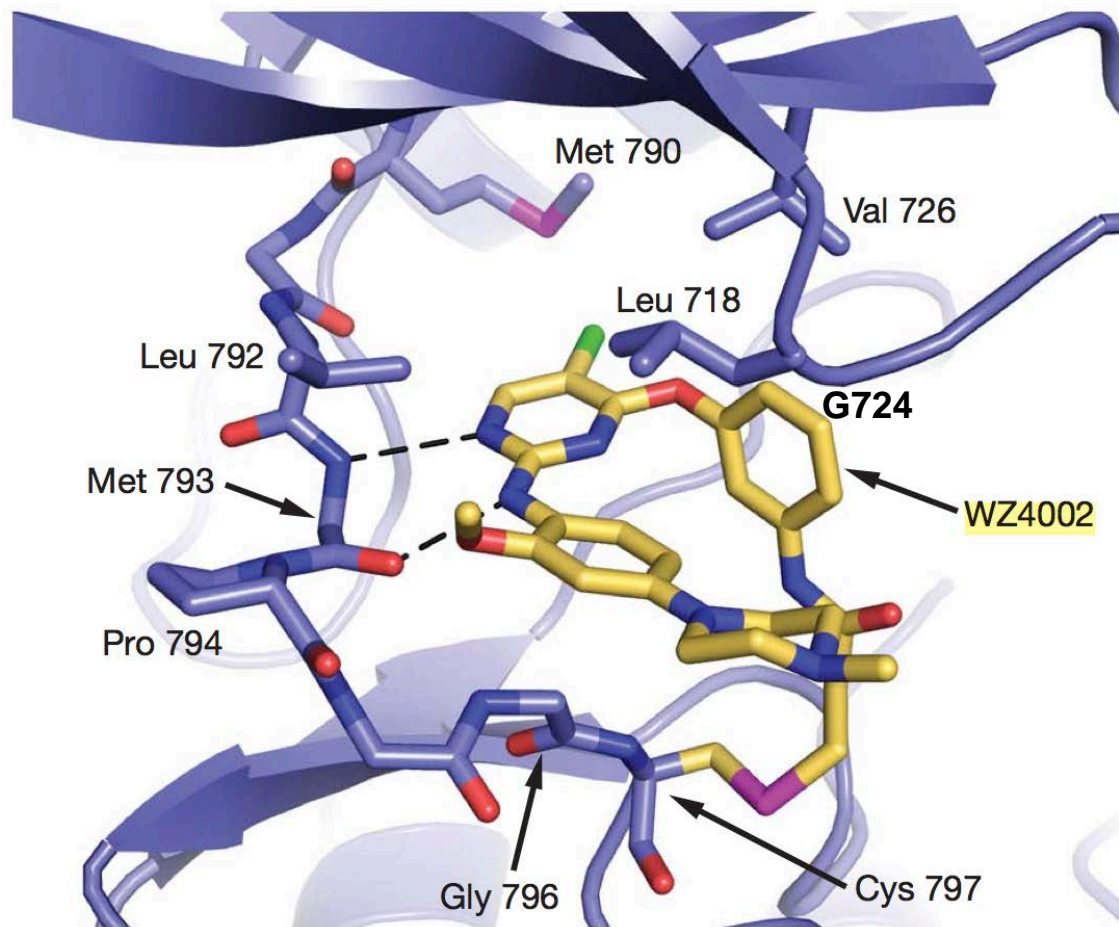
**10,2 (9,6; 11,1)**

**HR 0,46**

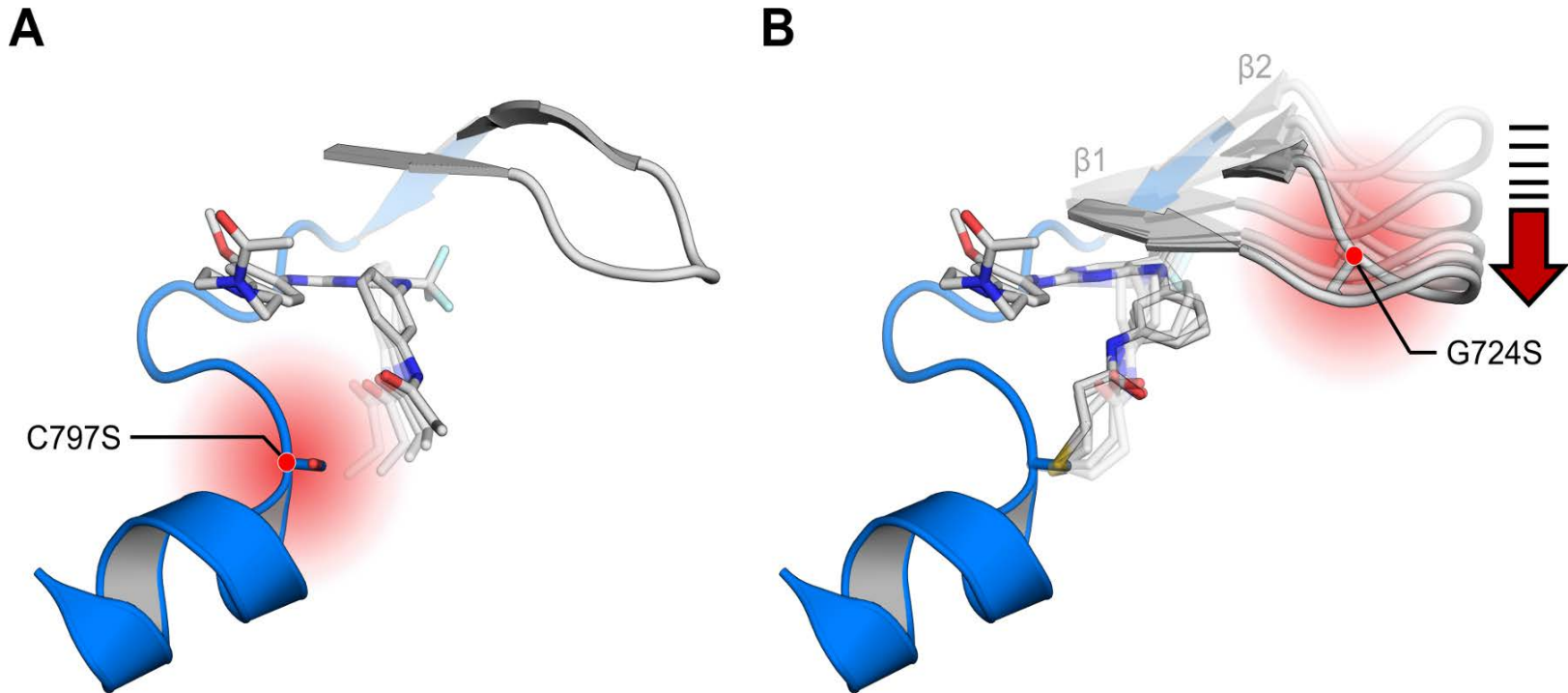
**(95%KI 0,37; 0,57)**

**p<0,0001**

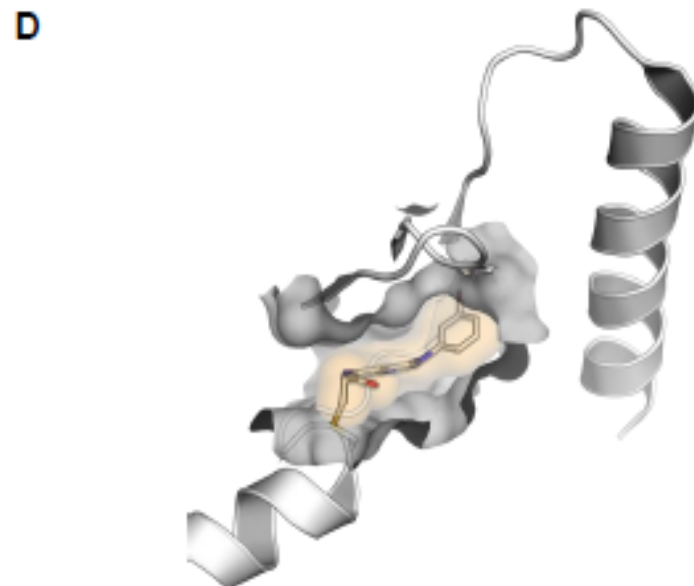
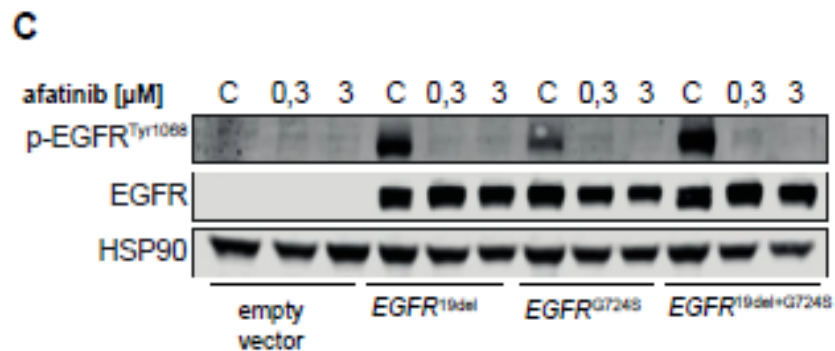
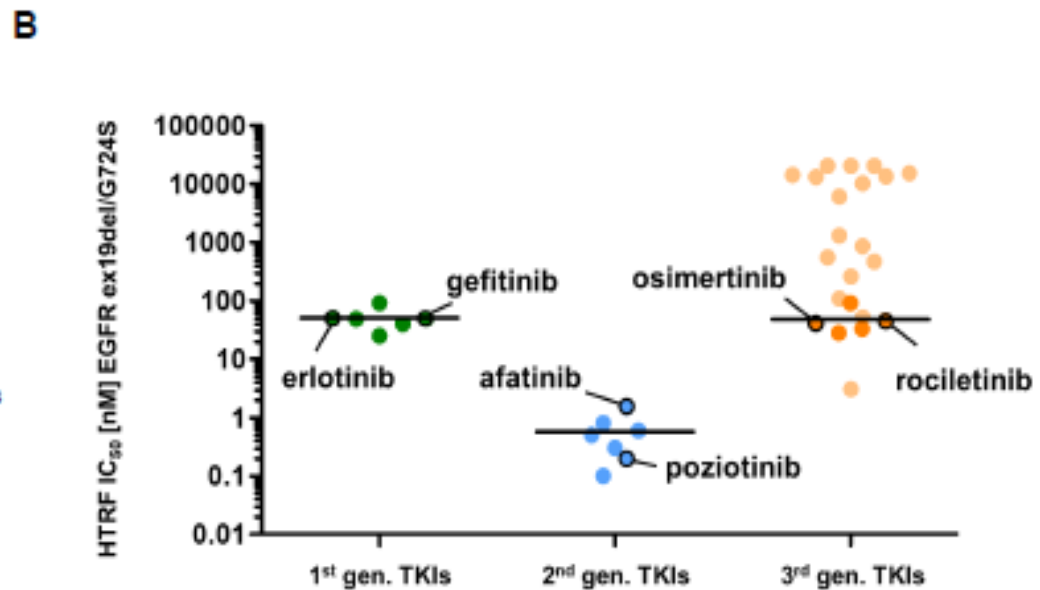
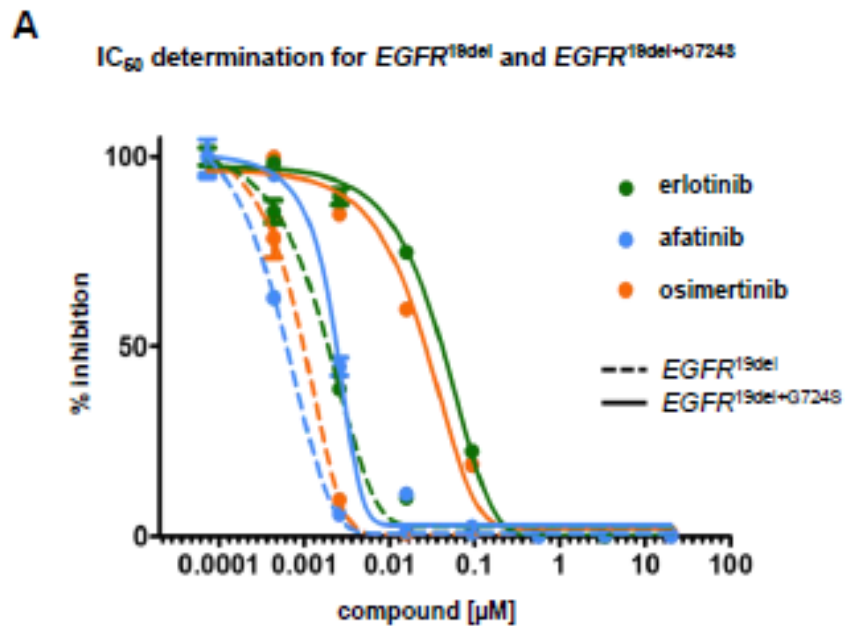
# Overcoming resistance by structure-based compound design



# EGFR<sup>G724S</sup> osimertinib resistance mutation sensitive to 2<sup>nd</sup> gen. EGFR inhibitor afatinib

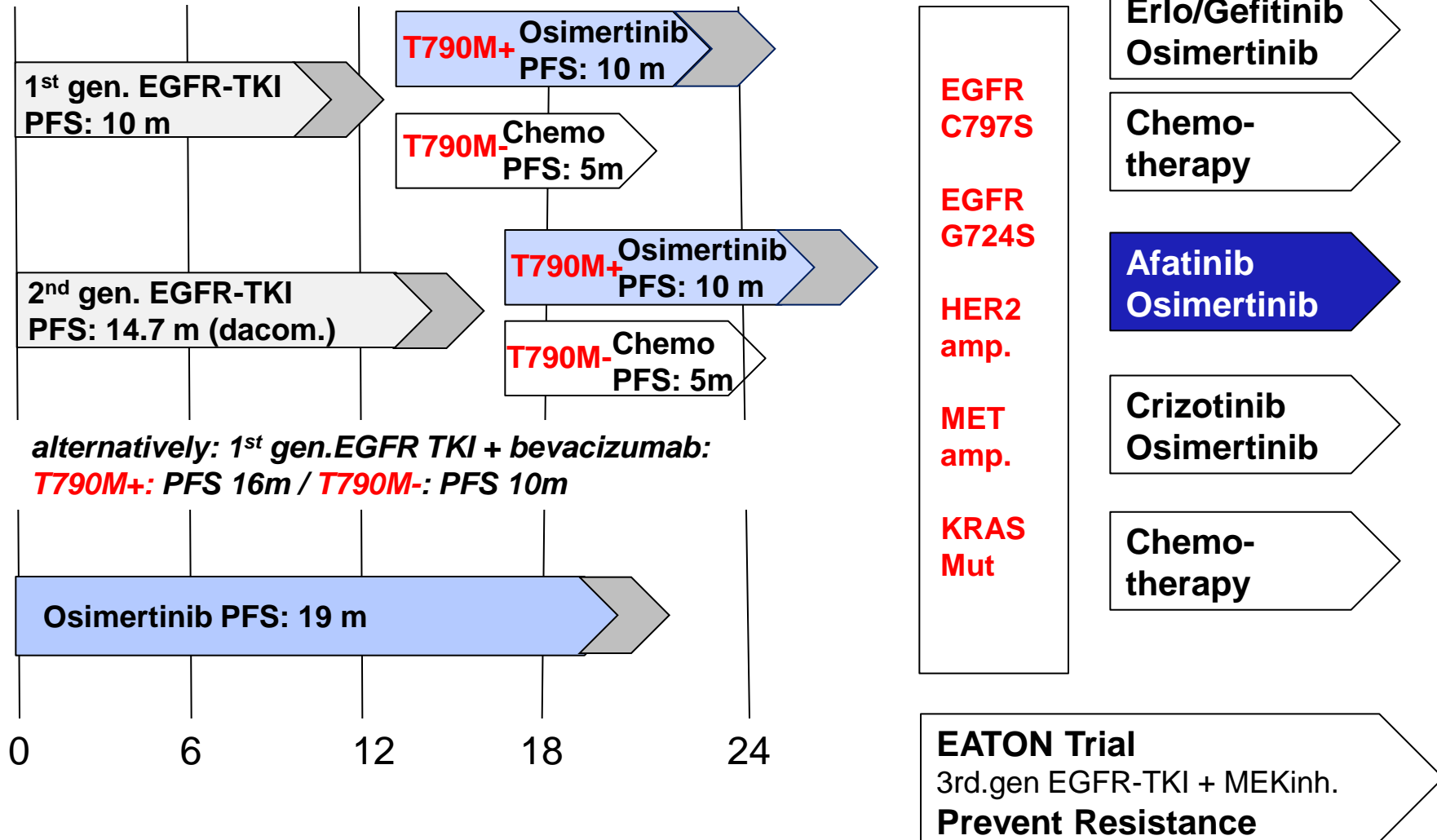


- Osimertinib first-line suppresses emerging T790M
- G724S and C797S are the most frequent resistant mutations after osimertinib.



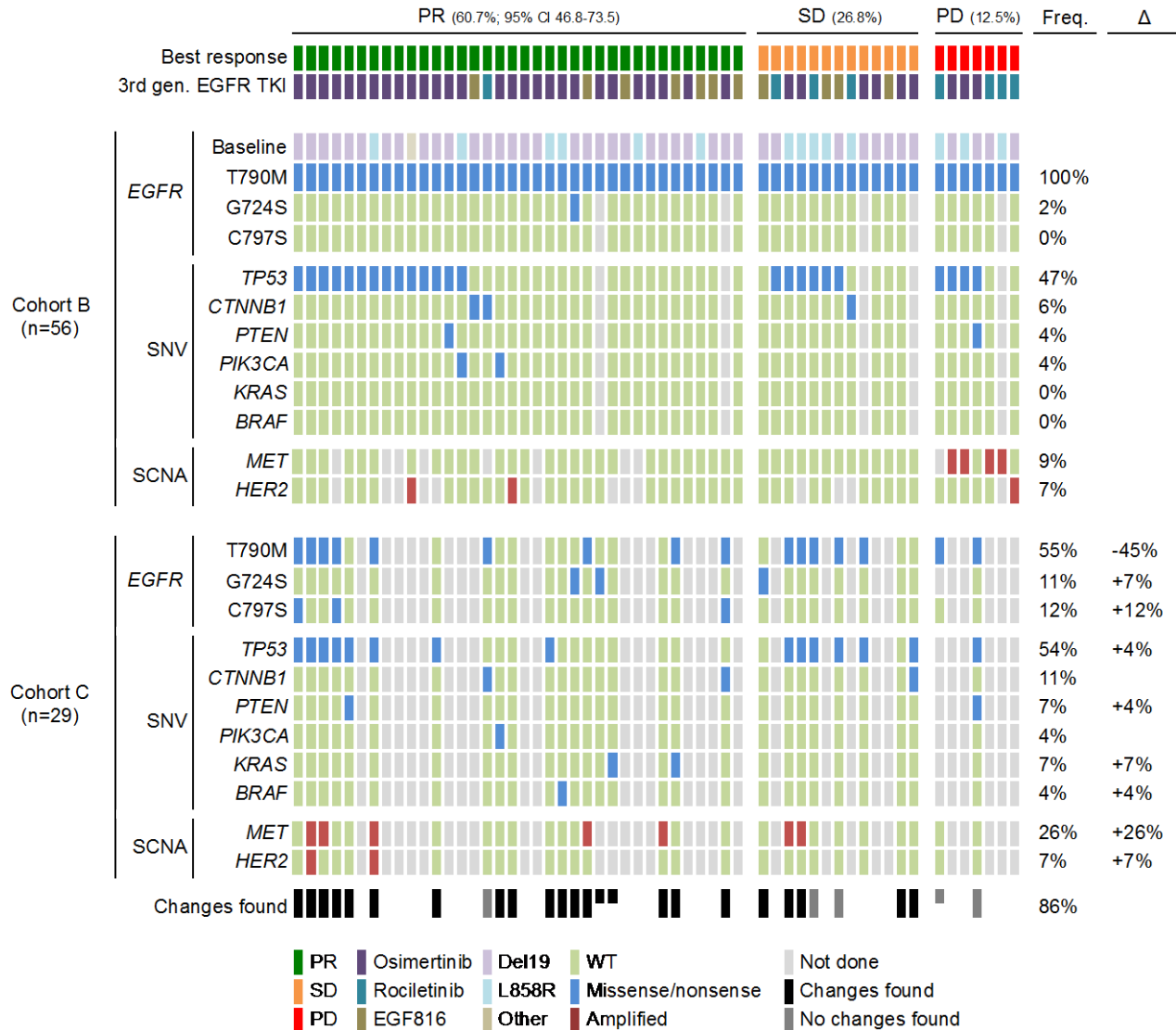
# Sequential therapy in EGFRmut NSCLC: increasingly molecularly guided

PD: rebiopsy

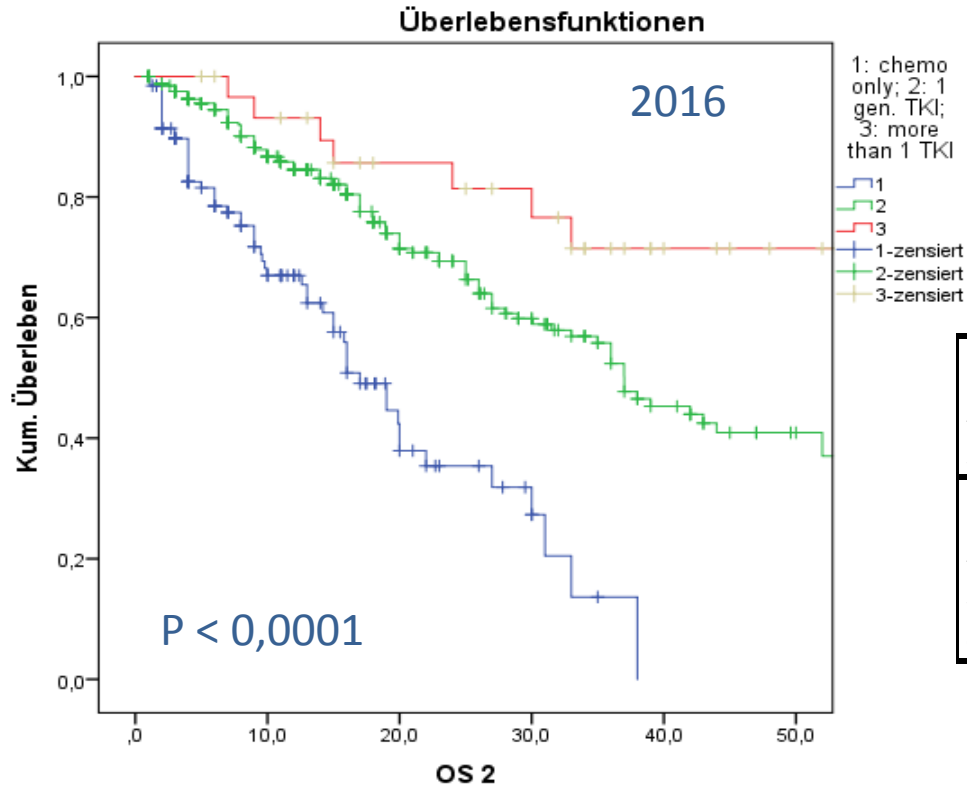




# Genomic profiling identifies outcome-relevant mechanisms of innate and acquired resistance to third-generation EGFR TKI therapy in lung cancer



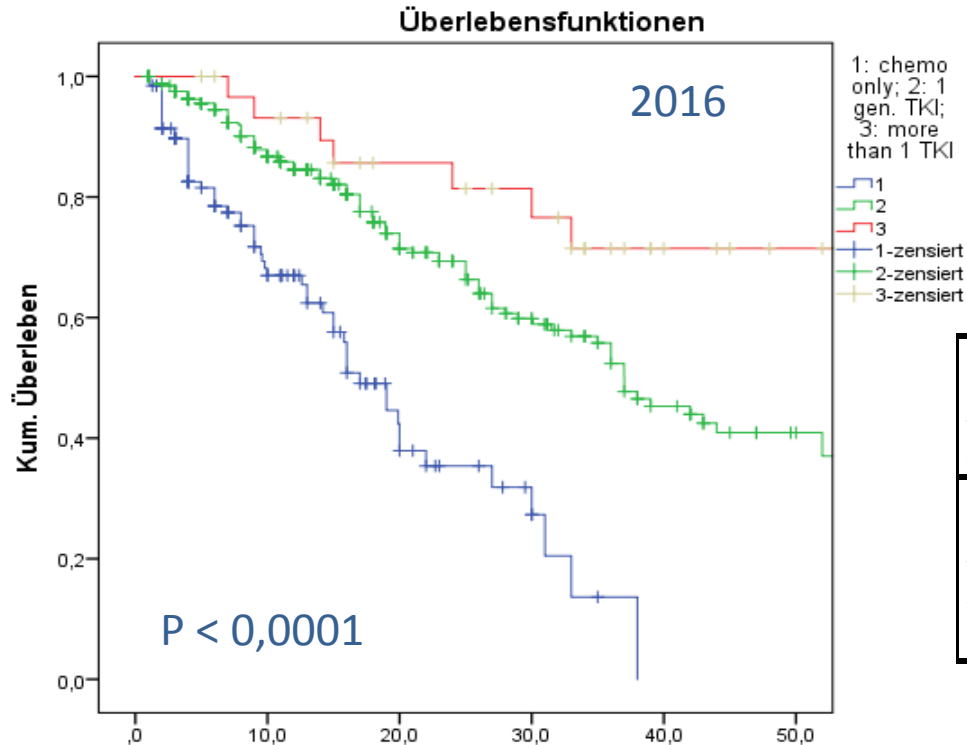
# EGFRmut. NGM cohort: overall survival dependent on therapy



1: chemo only; 2: 1 gen. TKI; 3: more than 1 TKI	Gesamtzahl	Anzahl der Ereignisse	Median in Monaten
1	129	57	17,000
2	335	103	37,000
3	31	8	56,000
<b>Gesamt</b>	<b>495</b>	<b>168</b>	<b>35,000</b>

3: 1<sup>st</sup> gen. EGFR-TKI followed by  
3<sup>rd</sup> gen. EGFR-TKI

# EGFRmut. NGM cohort: overall survival dependent on therapy



1: chemo only; 2: 1 gen. TKI; 3: more than 1 TKI	Gesamtzahl	Anzahl der Ereignisse	Median in Monaten
1	129	57	17,000
2	335	103	37,000
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<b>Gesamt</b>	<b>495</b>	<b>168</b>	<b>35,000</b>

Large Numbers in the nNGM Network

Combined Expertises of Tumor Biology, Chemical Biology, Molecular Pathology and Clinical Oncology

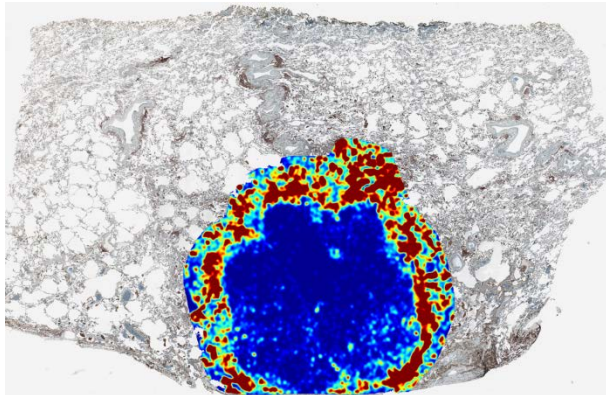
>>> Translate into Better Survival of Patients

>>> Translate into Innovation and New Therapies



nNGM

National Network  
Genomic Medicine  
Lung Cancer



Application of Artificial  
Intelligence (AI)  
Predicting Efficacy of  
Immune Therapies

**ImmunePredict**<sup>®</sup>  
Predicting Response to Immunotherapy



Network  
Genomic Medicine  
Lung Cancer

## **Innovative Clinical Trials**

**> treating small genetic lung cancer subgroups**

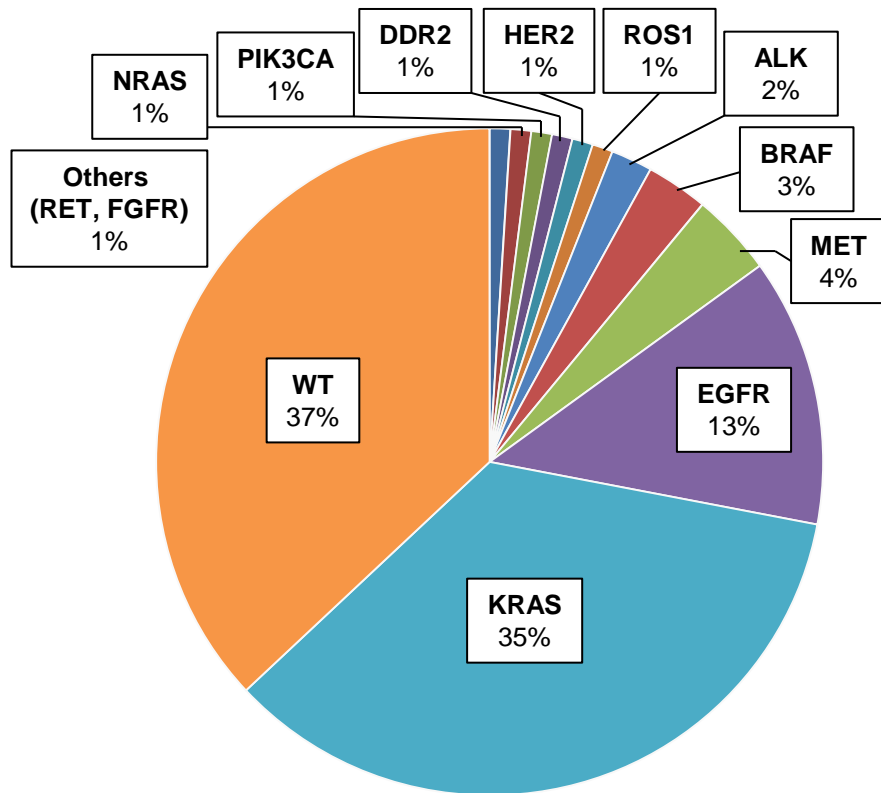
Sebastian Michels, Cologne – Medical Oncologist

Center for Integrated Oncology, University Hospital of Cologne

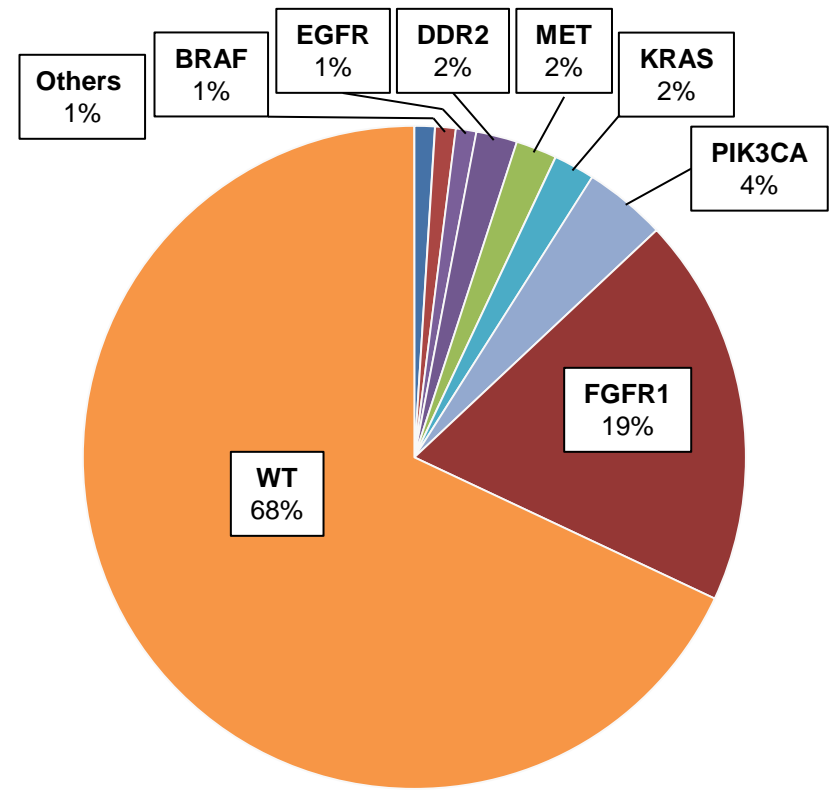
# Genetically-determined NSCLC subgroups

2<sup>nd</sup> evaluation of the Network Genomic Medicine (NGM, 2016)

Non-squamous NSCLC  
(n=4244)



Squamous NSCLC  
(n=1489)



## Publications of NGM subcohorts

MET: Schildhaus et al, Clin Cancer Res 2014; PIK3CA: Scheffler et al, Oncotarget 2014; ROS1: Scheffler et al, Oncotarget 2015; RET: Michels et al, J Thoracic Oncol 2016; KEAP1: Frank et al, Clin Cancer Res 2018; ALK: Kron et al, Annals of Oncology 2018; EGFR: Michels et al, JCO Precision Oncol 2018 (in press); RAS: Scheffler et al, under review; BRAF: Kron et al, in prep.

MET: Kron et al, in prep.

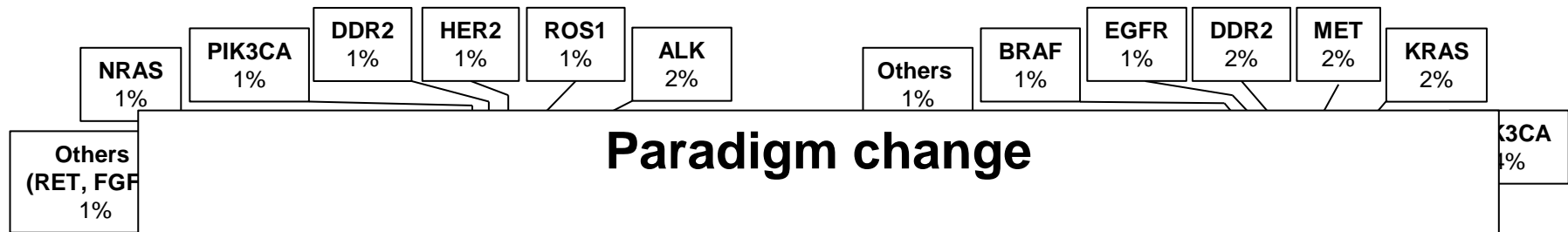


# Genetically-determined NSCLC subgroups

2<sup>nd</sup> evaluation of the Network Genomic Medicine (NGM, 2016)

Non-squamous NSCLC  
(n=4244)

Squamous NSCLC  
(n=1489)



## Paradigm change

Lung cancer is not one tumour, but many genetically-determined tumours of the lungs!

Treatment has been guided by these genetic aberrations since the discovery of EGFR inhibition in lung cancer.

More and more targeted drugs are being developed.

### Publications of NGM subcohorts

MET: Schildhaus et al, Clin Cancer Res 2014; PIK3CA: Scheffler et al, Oncotarget 2014; ROS1: Scheffler et al, Oncotarget 2015; RET: Michels et al, J Thoracic Oncol 2016; KEAP1: Frank et al, Clin Cancer Res 2018; ALK: Kron et al, Annals of Oncology 2018; EGFR: Michels et al, JCO Precision Oncol 2018 (in press); RAS: Scheffler et al, under review; BRAF: Kron et al, in prep.  
MET: Kron et al, in prep.

# Lung Cancer Group Cologne trial platform

“To treat each patient according to the genetic vulnerability of the tumour”

## Pharma trials/IITs of other groups

### FIM/phase I platform

EGFR - ALK - MET  
FGFR - RAS - IO

### Phase II/III platform

HER2 - IO - DLL3 -  
NTRK - ROS1

### LCGC lead trials

MET (INC280)  
FGFR (BGJ398)

## Translational program

Pathology - AG Thomas - AG Sos - AG Ulrich - AG Pfeifer - AG vBergwelt

## LCGC/NGM IIT platform

### Rare entity trial platform

ROS1 (EUCROSS) - HER2 (TRY) - FGFR  
(FIND) - MET (TransMET)

### EGFR program

EATON - EGFR database - rebiopsy program

### IO program

BIOLUMA - rebiopsy program

### SCLC program (under construction)

Rebiopsy program - SFB

## **ROS1 rearrangement in lung cancer**

Very rare and predominantly in young never-smokers

**First evidence, that the small-molecule inhibitor crizotinib was effective in ROS1-positive lung cancer (2012)!**



How to ensure treatment access to ROS1 patients?

How to systematically prove the efficacy of crizotinib in these patients?

# Crizotinib in ROS1-positive NSCLC

## EUCROSS trial: Overview and challenges

### Hypothesis

Crizotinib is effective and safe in ROS1-positive lung cancer (N=30 patients)

# Crizotinib in ROS1-positive NSCLC

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### Management team

LCGC, CTCC, SLCG

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### Financial support

Pfizer

### Drug supply

Pfizer

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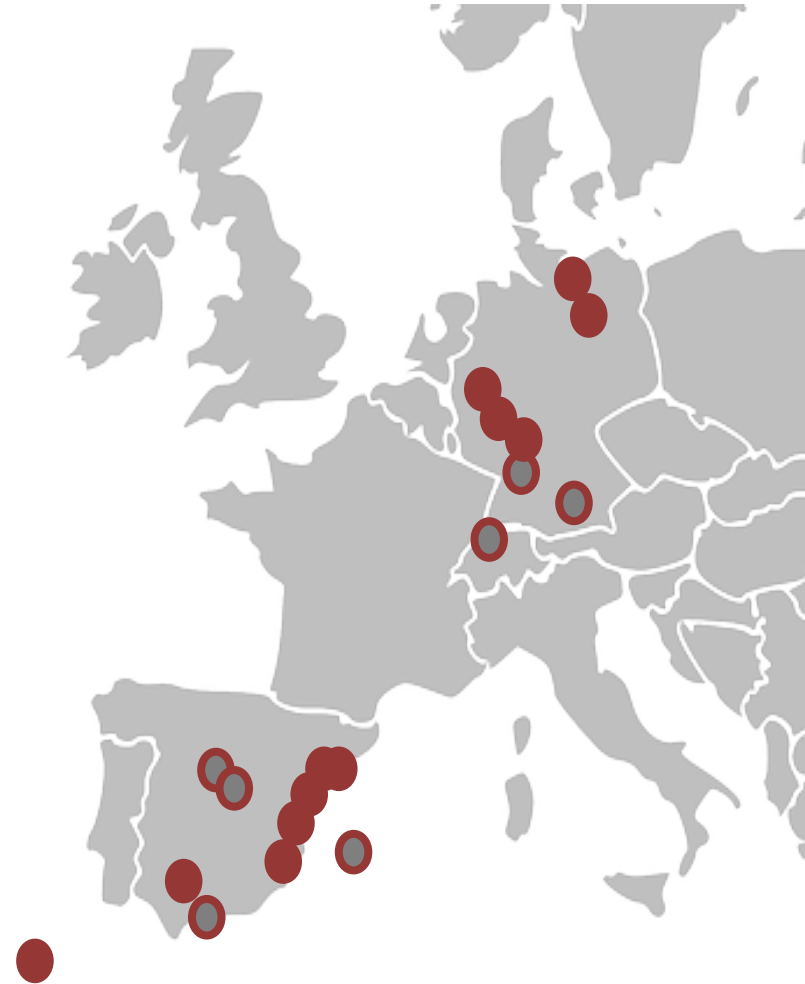
Pfizer

### Drug supply

Pfizer

### Sites

LCGC, SLCG, collaborating centers





# Crizotinib in ROS1-positive NSCLC

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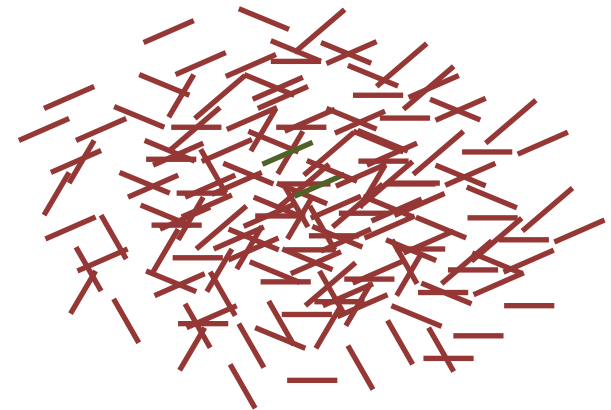
### Screening platform

Network Genomic Medicine (NGM)

**6000 patients screened**

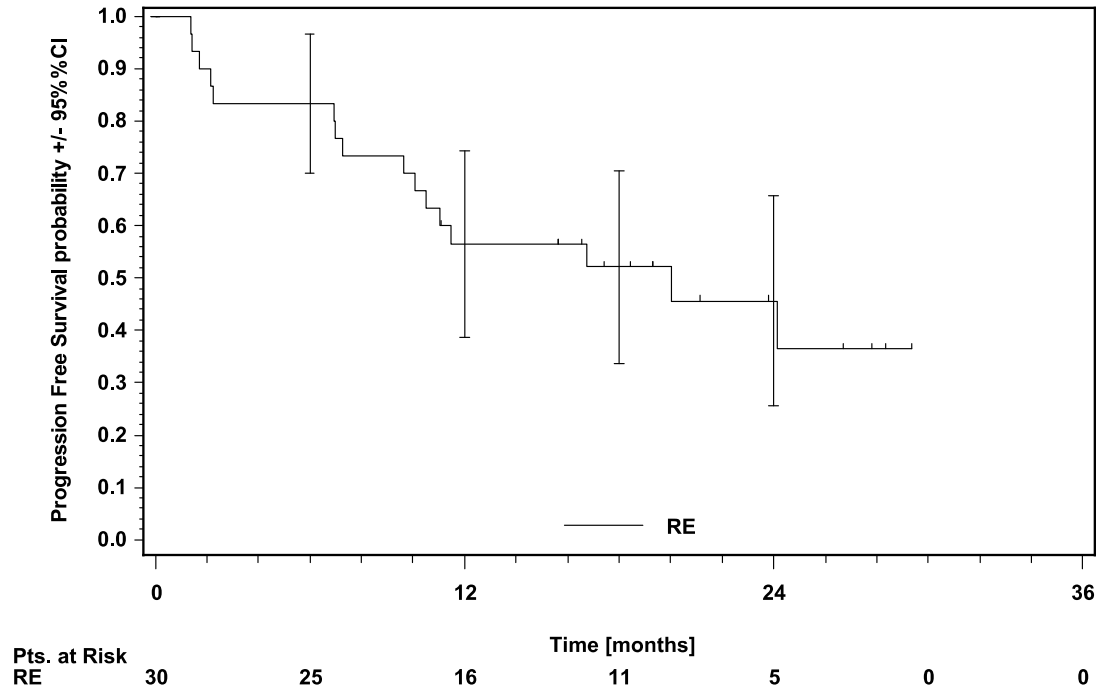
50% drop out rate

30 ROS1-positive



# Crizotinib in ROS1-positive NSCLC

## EUCROSS trial: Efficacy

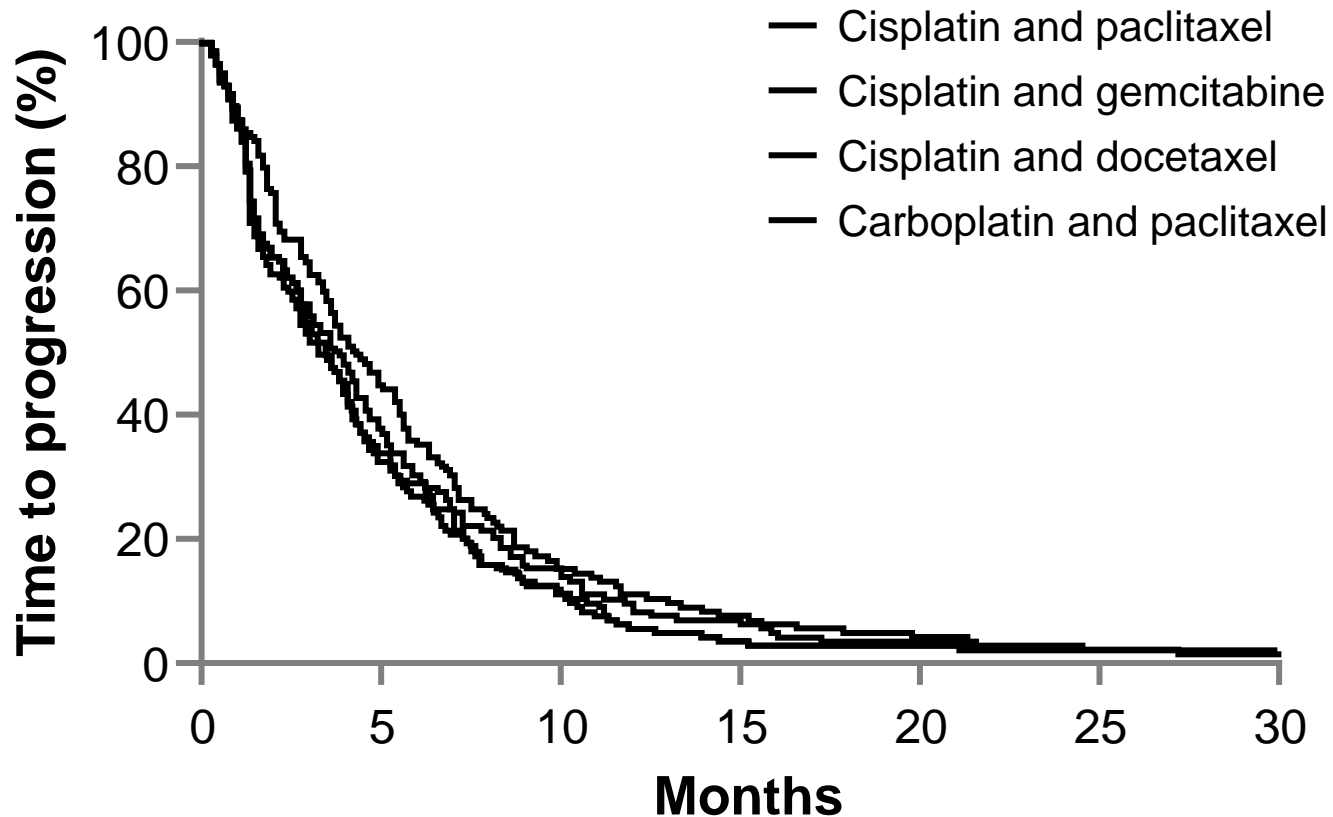


**Fig.:** KM-analysis of progression-free survival (n=30)

	Local assessment	BIRC
ORR (%)	70.0 (n=21; 95% CI, 50.6-85.3)	72.4 (n=21; 95% CI, 52.3-87.3)
Median PFS (months)	20.0 (95% CI, 10.09-n.r.)	20.0 (95% CI, 9.6-NR)
PFS at 24 months (%)	45.6 (95% CI, 25.6-65.6)	45.8 (95% CI, 25.8-65.8)

# Efficacy of chemotherapy in lung cancer

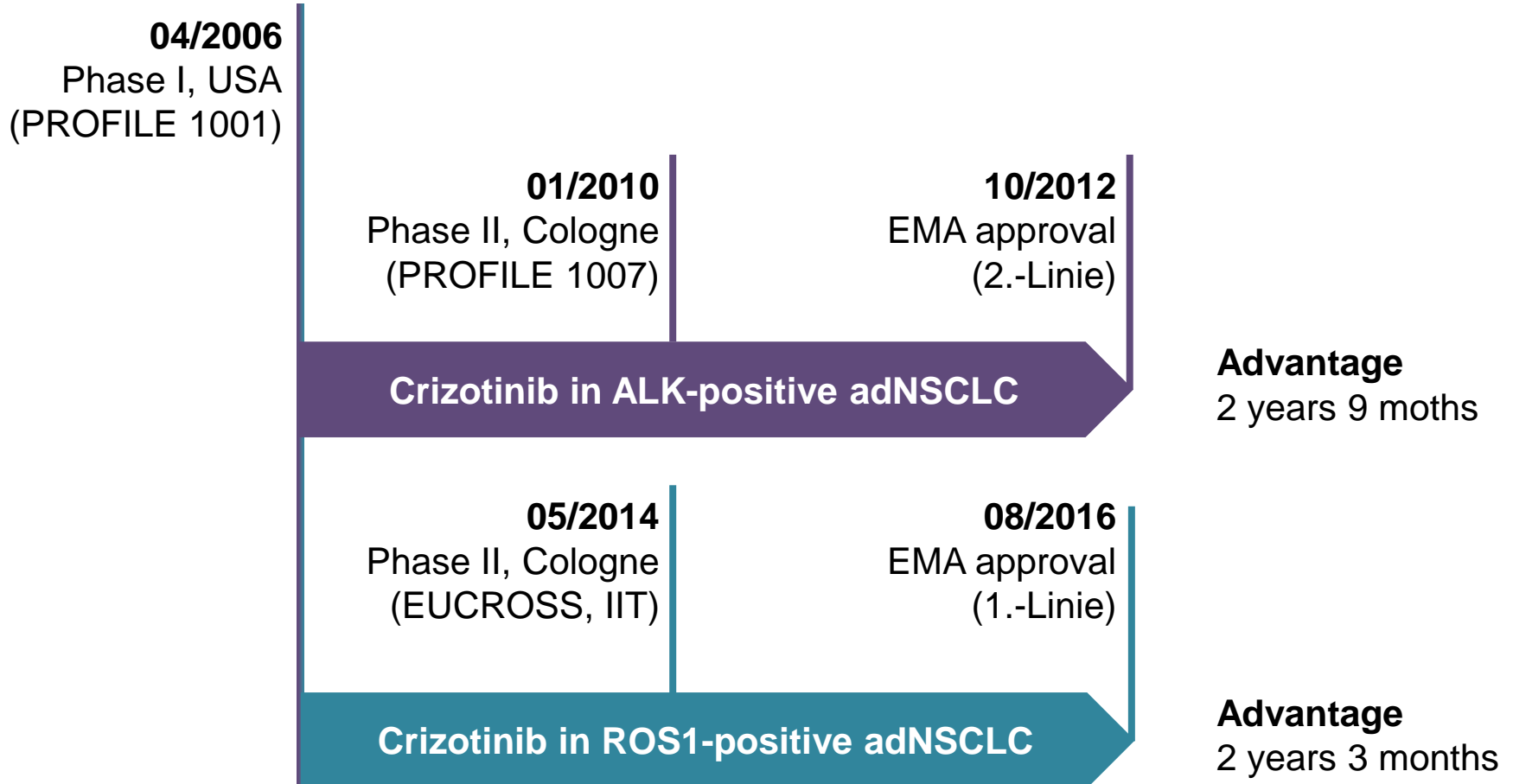
Only approved treatment at the time of EUCROSS initiation



ORR: 17-22%  
PFS: 3.1-4.2 months  
2-year survival: 10-13%

# Advantage of early trial participation

Patients received crizotinib treatment in clinical trials years before approval



# Structure of the LCGC/NGM IIT platform

## Financial sponsors

Pharmaceutical companies • Public sponsors

### LCGC

Conceptional/hypothesis formation • Protocol writing • Project management

### Cooperating platforms

Spanish Lung Cancer Group • ETOP • AIO

### CTC Cologne/ZKS Köln

Project management  
Database provision  
Monitoring • SAE management

### Screening platform

NGM/nNGM  
Cooperating platforms

### Trial sites

NGM sites • Non-NGM sites • Cooperating platforms

### Translational program

Pathology • AG Thomas • AG Sos • AG Ulrich • AG Pfeifer • AG vBergwelt

### LCGC IITs and projects

ERLOPET • TransMET • TRY • EUCROSS • BIOLUMA • EATON • FIND

# Structure of the LCGC/NGM IIT platform

ic sponsors

## LCGC

Conceptional/hypothesis formation • Protocol writing • Project management

## Cooperating platforms

Spanish Lung Cancer Group • ETOP • AIO

**These structures enable the fast development of clinical trials...**

...to treat lung cancer according to the underlying genetic aberration

...to allow patients early access to innovative drugs

...to allow proof-of-concept

...to develop new treatment approaches for small genetic subgroups

Financial sponsors  
Pharmaceutical

## Translational program

Pathology • AG Thomas • AG Sos • AG Ulrich • AG Pfeifer • AG vBergwelt

## LCGC IITs and projects

ERLOPET • TransMET • TRY • EUCROSS • BIOLUMA • EATON • FIND



Network  
Genomic Medicine  
Lung Cancer

## **Network Organization and IT Strategy**

Anna Kron, Cologne – Health Economist

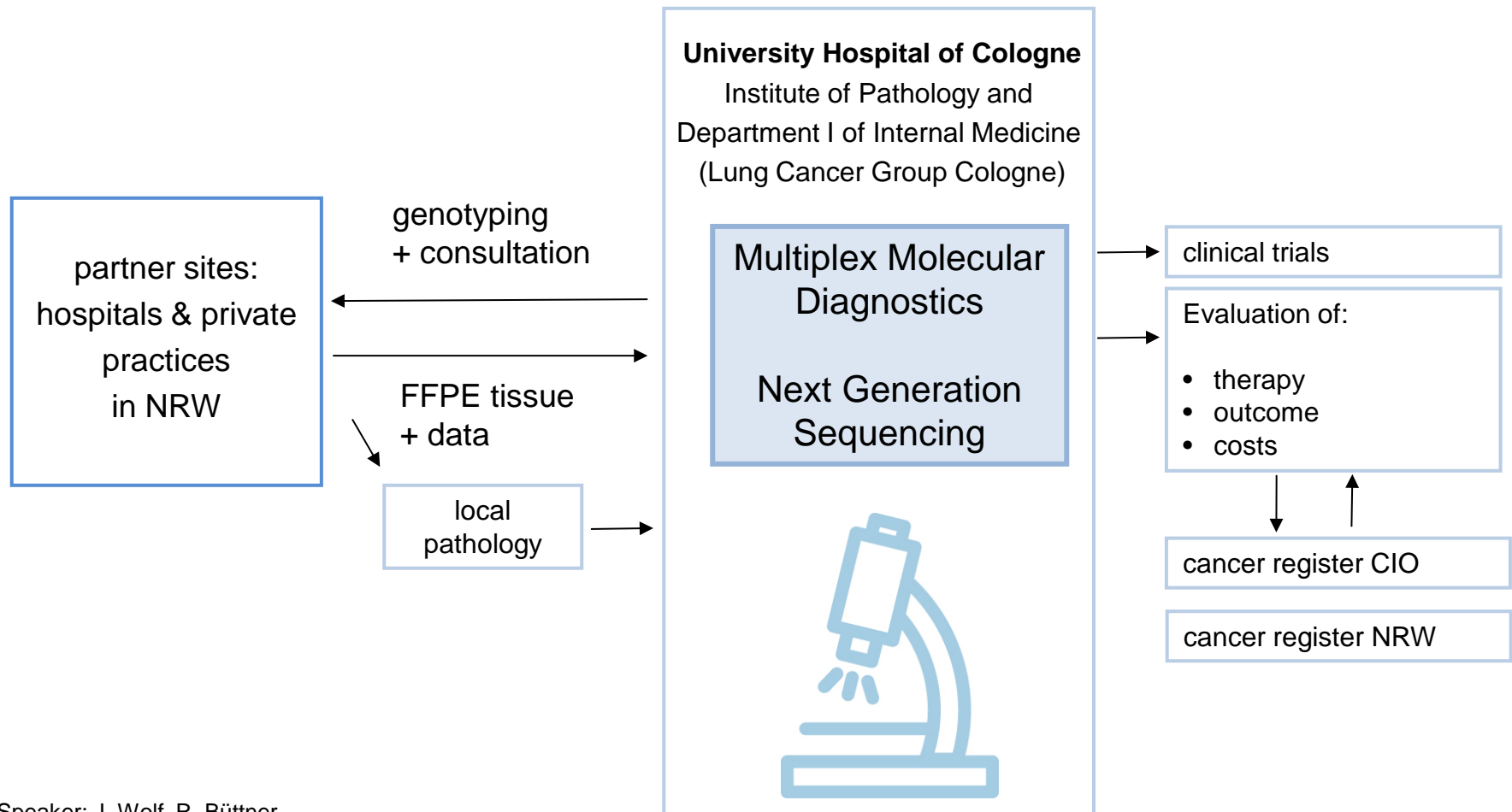
Center for Integrated Oncology, University Hospital of Cologne



# Network Genomic Medicine (NGM)



Founded in 2010 with funding from Ministry for Innovation and Research NRW



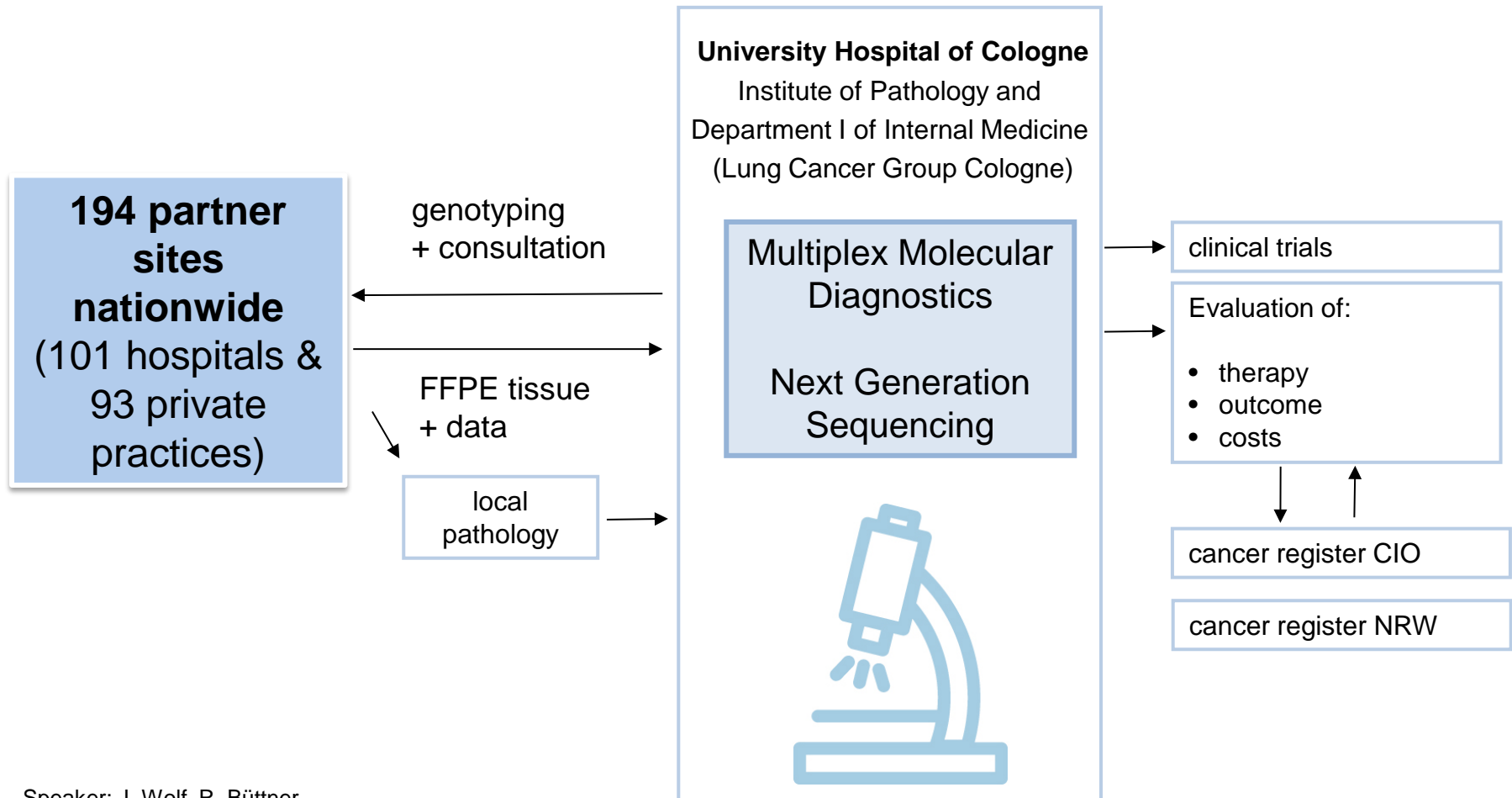
Speaker: J. Wolf, R. Büttner  
Scientific Coordinator: A. Kron, S. Michels

CLCGP & NGM, Sci Transl Med 2013, Scheffler et al., Oncotarget 2014, Schildhaus et al., Clin Cancer Res 2015, Scheffler et al., Oncotarget 2015, Michels et al., JTO

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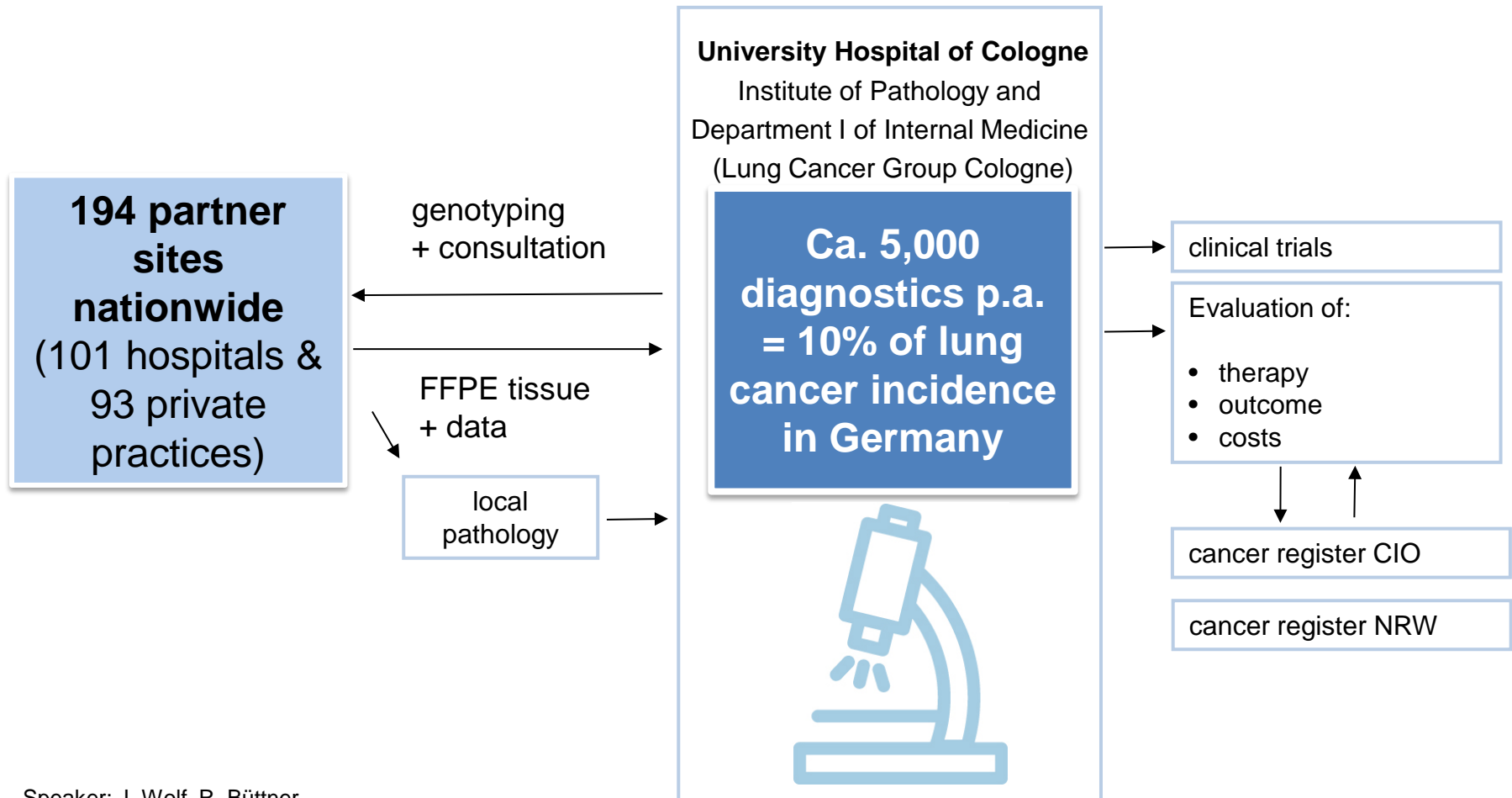
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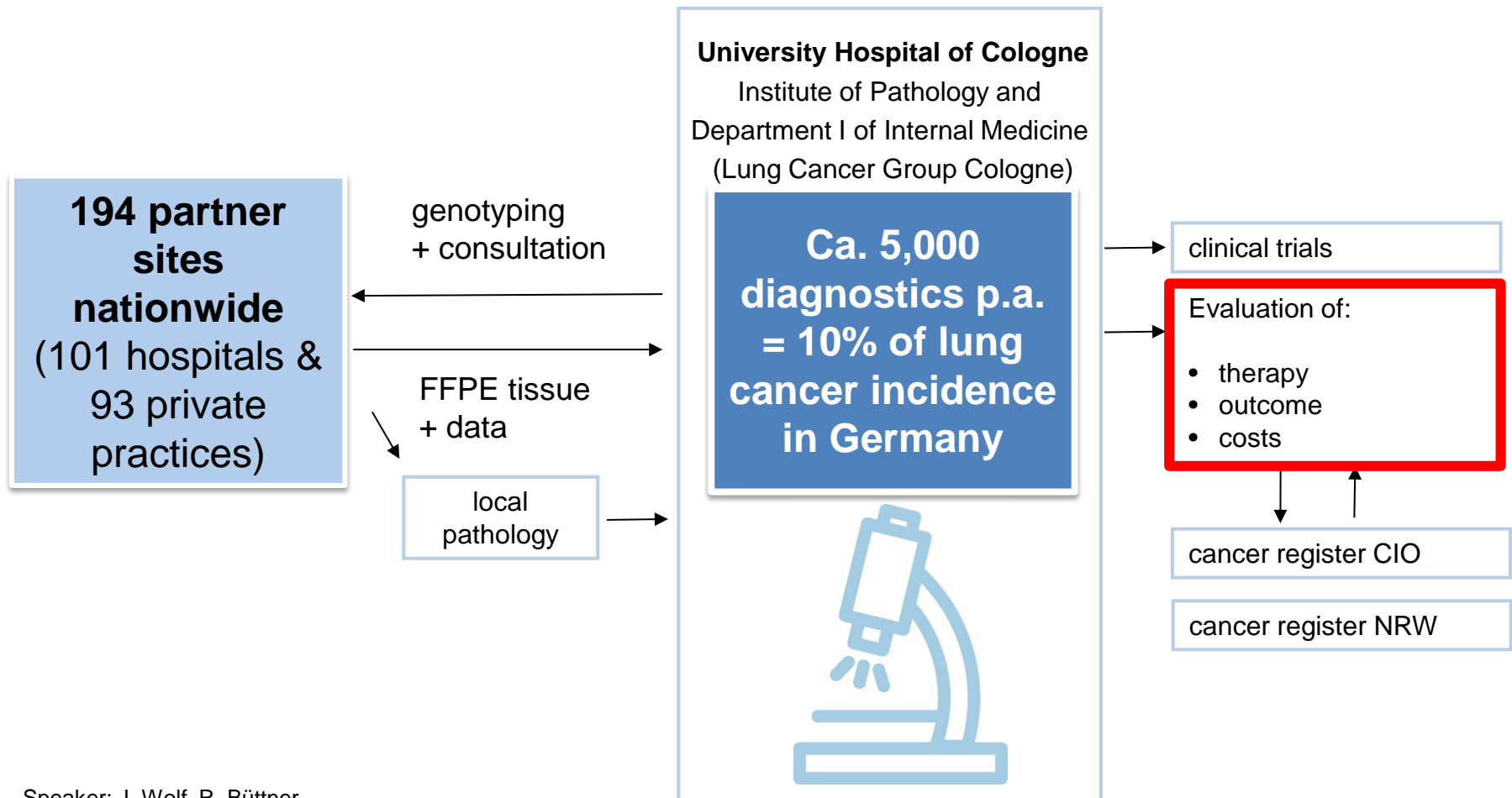
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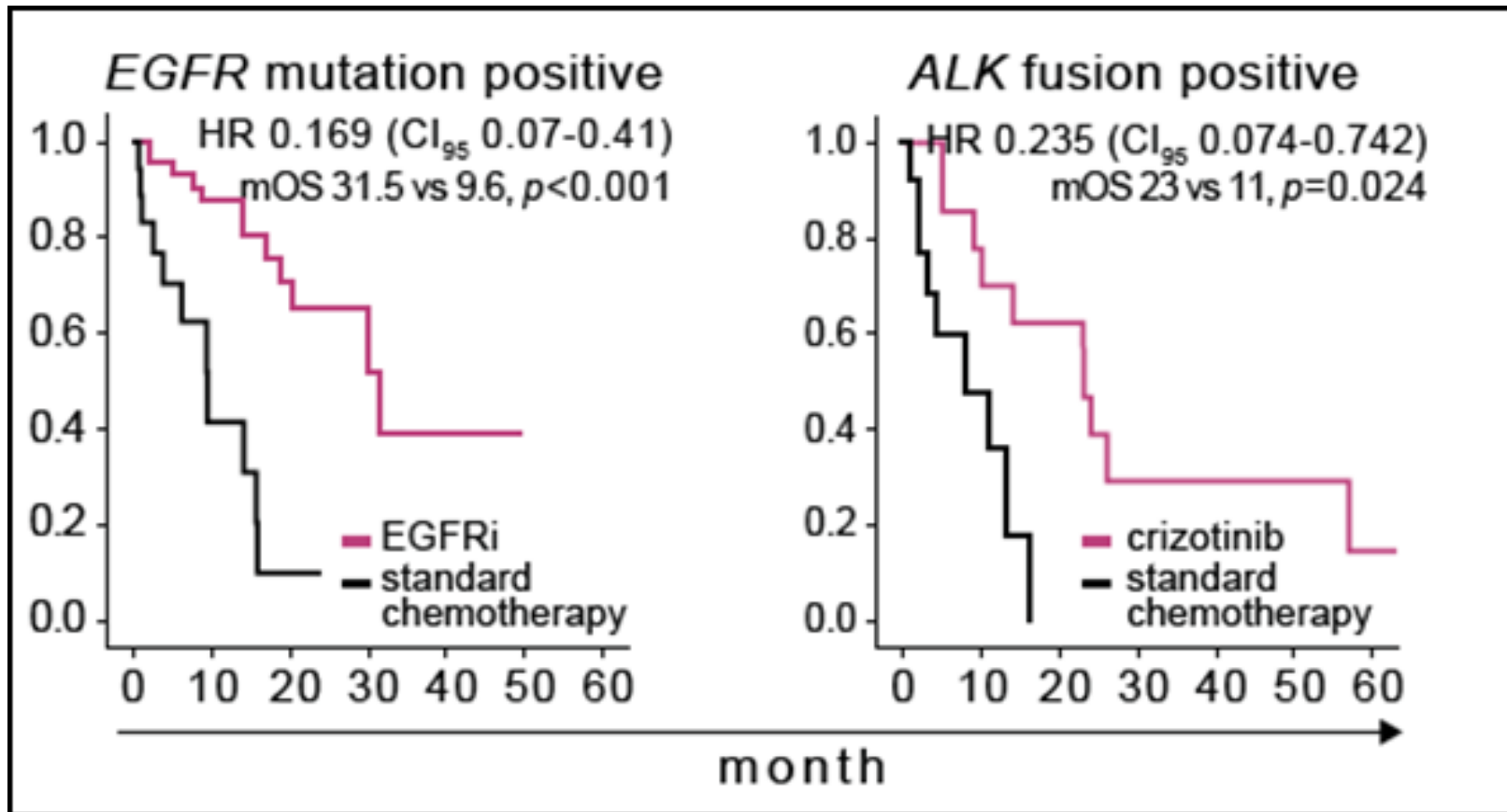
CLCGP & NGM, Sci Transl Med 2013, Scheffler et al., Oncotarget 2014, Schildhaus et al., Clin Cancer Res 2015, Scheffler et al., Oncotarget 2015, Michels et al., JTO

# 1st NGM Evaluation 2013:

## OS benefit with personalized therapies



Network  
Genomic Medicine  
Lung Cancer



# Integrated Care Contract (ICC)

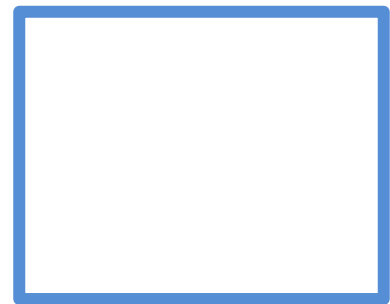


Network  
Genomic Medicine  
Lung Cancer



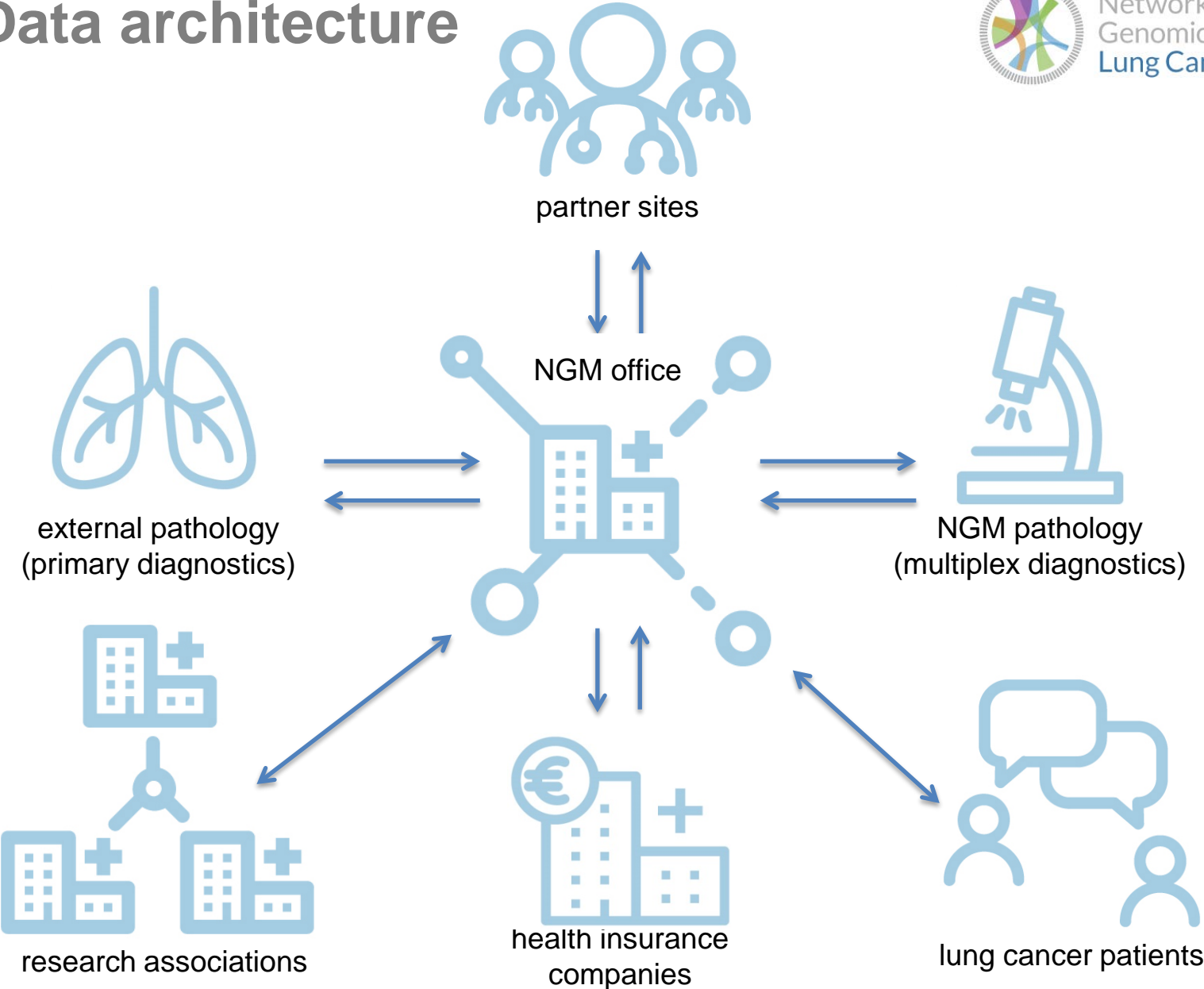
NGS-based genotyping + consultation potentially covered by ICC for ca. 53% of all annually newly diagnosed inoperable lung cancer patients in Germany





[ngm-cancer.com/aerzte-in-ihreer-naehe/](https://ngm-cancer.com/aerzte-in-ihreer-naehe/)

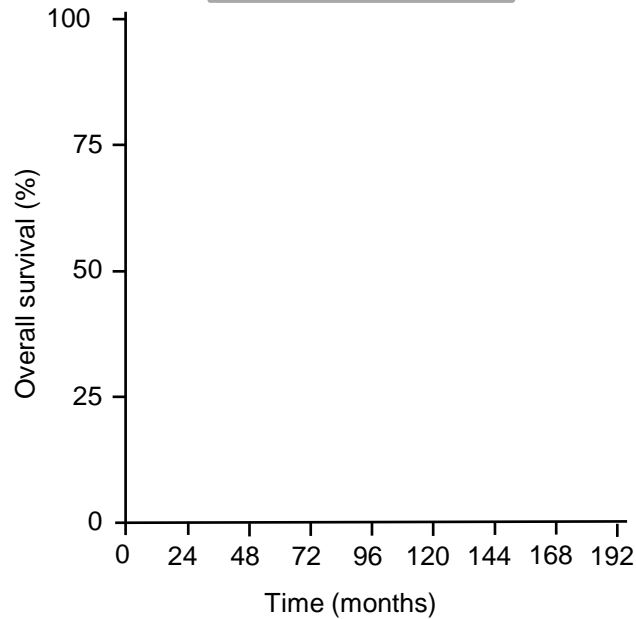
# Data architecture



# 2nd NGM Evaluation 2018:

## OS benefit with sequential therapies

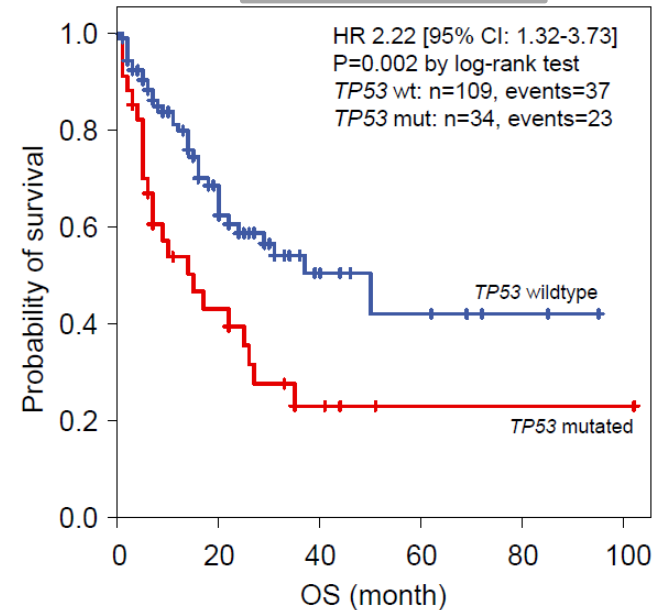
**EGFR+**



N° at risk:

Wt	43	39	19	6	3	1	1	1	0
Ampl.	4	1	0	0	0	0	0	0	0

**ALK+**



TP53 wt	109	44	11	5	2	0
TP53 mut	34	12	4	1	1	1

# Conclusions



- **NGM = established network model for implementation of NGS-based diagnostics and personalized therapy**
- **Sufficient reimbursement supports innovation transfer into clinical practice**
- **Networked data = major challenge and main opportunity for evidence-based treatment**
- **NGM goes nNGM**



Molekularpathologie

### Aktuelles



#### Das nNGM hat eine neue Webseite!

Nov 9, 2018 | Ärzte, Veranstaltungen  
Das nationale Netzwerk Genomische Medizin (nNGM) präsentiert seine neue Webseite: [www.ngm.de](http://www.ngm.de). Die Zentren des nNGM-Verband haben seit letzter Woche ein gemeinsames Zuhause im Web. Auf der Webseite stellt sich das nNGM mit seinen Mitgliedern und regionalen...



#### NEUE Studie: Eine multizentrische, offene Phase-I Dosisesskalations-Studie mit EGF816 und Trametinib bei Patienten mit nicht-kleinzelligem Bronchialkarzinom und EGFR p.T790M vermittelter Resistenz auf EGFR Inhibitoren der 1. und 2. Generation

Sep 25, 2018 | Ärzte, Veranstaltungen  
Eine multizentrische, offene Phase-I Dosisesskalations-Studie mit EGF816 und Trametinib bei Patienten mit nicht-



Nationales Netzwerk Genomische Medizin Lungenkrebs



#### Projektstart für das Nationale Netzwerk Genomische Medizin (nNGM) ab dem 01.04.2018

Apr 4, 2018 | Ärzte, Veranstaltungen  
Start des Verbundprojekts "nationales Netzwerk Genomische Medizin (nNGM)" zum 01.04.2018  
Eine Förderung der Deutschen Krebshilfe über ein bundesweites Netzwerk sollen in Deutschland künftig alle Patienten mit fortgeschrittenem



#### Finden Sie Ärzte in Ihrer Nähe

Im NGM arbeiten Krankenhäuser und Facharztpraxen interdisziplinärer Fachrichtungen sektorübergreifend zusammen.  
Finden Sie den Netzwerkkooperationspartner in Ihrer Nähe.

Ärzteverzeichnis



#### Fordern Sie die Diagnostik an

Das NGM bietet mittels Next Generation Sequencing eine umfassende molekulare Analyse von Tumorproben an und detektiert zuverlässig sämtliche therapierelevante genomische Veränderungen auch in kleinsten Gewebeproben.  
Als Partner des NGM faxen Sie uns einfach den Anforderungsschein inkl. Patienteneinwilligung/Teilnahmeerklärung zu:

Fax: 0221-478-1460207

Anforderungsschein



#### Werden Sie Mitglied

Als klinischer Kooperationspartner des Integrierten Versorgungsvorganges haben Sie die Möglichkeit, die umfangreiche molekular-pathologische Diagnostik für Ihre Patienten im Institut für Pathologie am Universitätsklinikum Köln anzufordern.

Mitgliedschaft

## Studienübersicht

Kurzbezeichnung	Titel	Indikation	Marker	Status
CEGF816X2102	Eine multizentrische, offene Studie der Phase Ib zur Charakterisierung der Sicherheit, Verträglichkeit und zur Erfassung erster Daten zur Wirksamkeit von EGF816 in Kombination mit ausgewählten zielgerichteten Wirkstoffen bei EGFR mutiertem NSCLC	Dies ist eine multizentrische, offene, nicht-randomisierte Dosiserweiterungsstudie der Phase Ib mit EGF816 in Kombination mit Ribociclib, Trametinib oder LXH254 gefolgt von einer Dosiserweiterung mit EGF816 in Kombination mit Ribociclib, Trametinib, LXH254, INC280 oder Gefitinib bei erwachsenen Patienten mit fortgeschrittenem EGFR mutiertem NSCLC.	EGFR	Aktive Studie
EATON	Eine multizentrische, offene Phase-I Dosiserweiterungs-Studie mit EGF816 und Trametinib bei Patienten mit nicht-kleinzelligem Bronchialkarzinom und EGFR p.T790M vermittelter Resistenz auf EGFR-Inhibitoren der 1. und 2. Generation	Patienten mit fortgeschrittenen oder metastasierten EGFR-mutiertem (EGFR del19,EGFR p.L858R) nicht-kleinzelligem Bronchialkarzinom. Eine durch EGFR p.T790M vermittelte Resistenz auf die Therapie mit EGFR-Inhibitoren der 1. und 2. Generation muss nachgewiesen sein. Die Tumoren der Patienten dürfen darüberhinaus keine „high-level“ Amplifikation des MET-Gens ausweisen.	EGFR	Aktive Studie

### Studie finden

Genmutation (Marker)

Bitte auswählen

Finden

## CEGF816X2102

Status: Aktive Studie | Marker: EGFR

### Titel

Eine multizentrische, offene Studie der Phase Ib zur Charakterisierung der Sicherheit, Verträglichkeit und zur Erfassung erster Daten zur Wirksamkeit von EGF816 in Kombination mit ausgewählten zielgerichteten Wirkstoffen bei EGFR mutiertem NSCLC

Zentrale Studiennummer

Indikation

Studienziel & Fragestellung

Patientenmerkmale

Studiendesign

Zuständigkeiten der Gesamtstudie

### Studie finden

Genmutation (Marker)

Bitte auswählen

Finden

### Suche

Suche

### News-Kategorien

Ärzte (7)

Patienten (1)

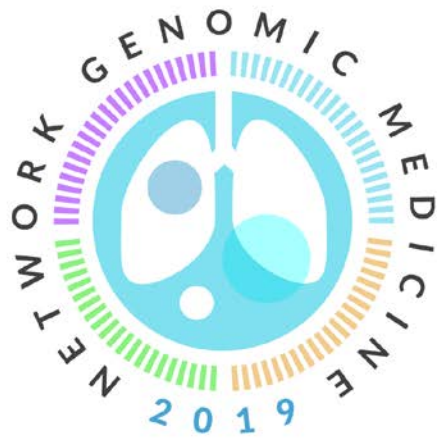
Veranstaltungen (3)

### Aktuelle Beiträge

Das nNGM hat eine neue Webseite!

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# SAVE THE DATE: 2<sup>nd</sup> Cologne Conference on Lung Cancer



## 2nd Cologne Conference on Lung Cancer

26 - 27 JUNE 2019 | GERMANY

[www.cologne-clc.com](http://www.cologne-clc.com)



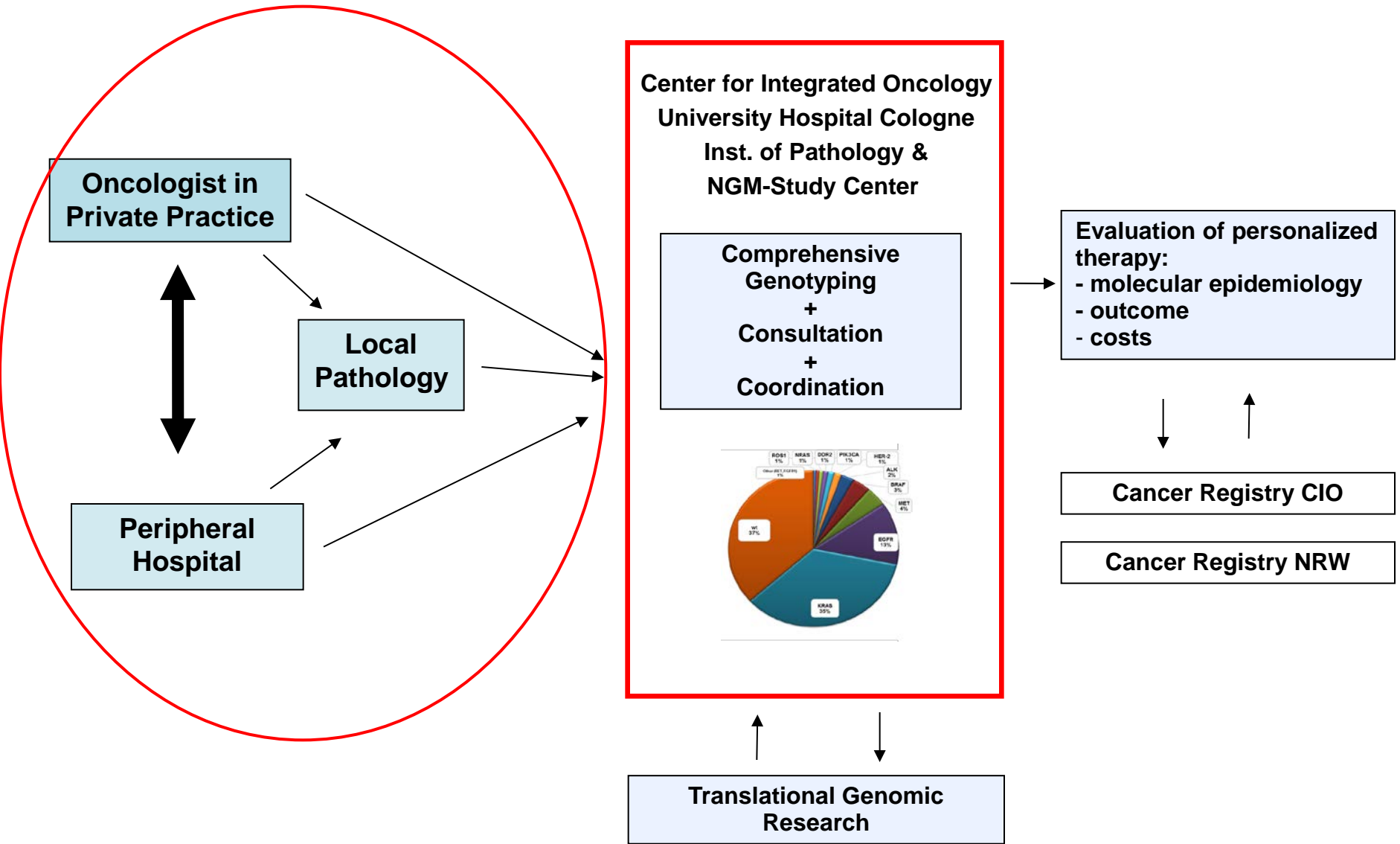


Network  
Genomic Medicine  
Lung Cancer

## The Referring Doctor's Strategy

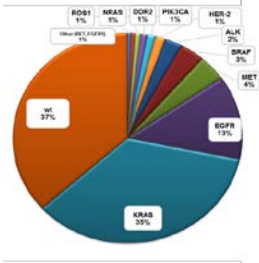
Achim Rothe, Cologne – Med. Oncologist in Private Practice

# Regional lung cancer network



Center for Integrated Oncology  
University Hospital Cologne  
Inst. of Pathology &  
NGM-Study Center

Comprehensive  
Genotyping  
+  
Consultation  
+  
Coordination



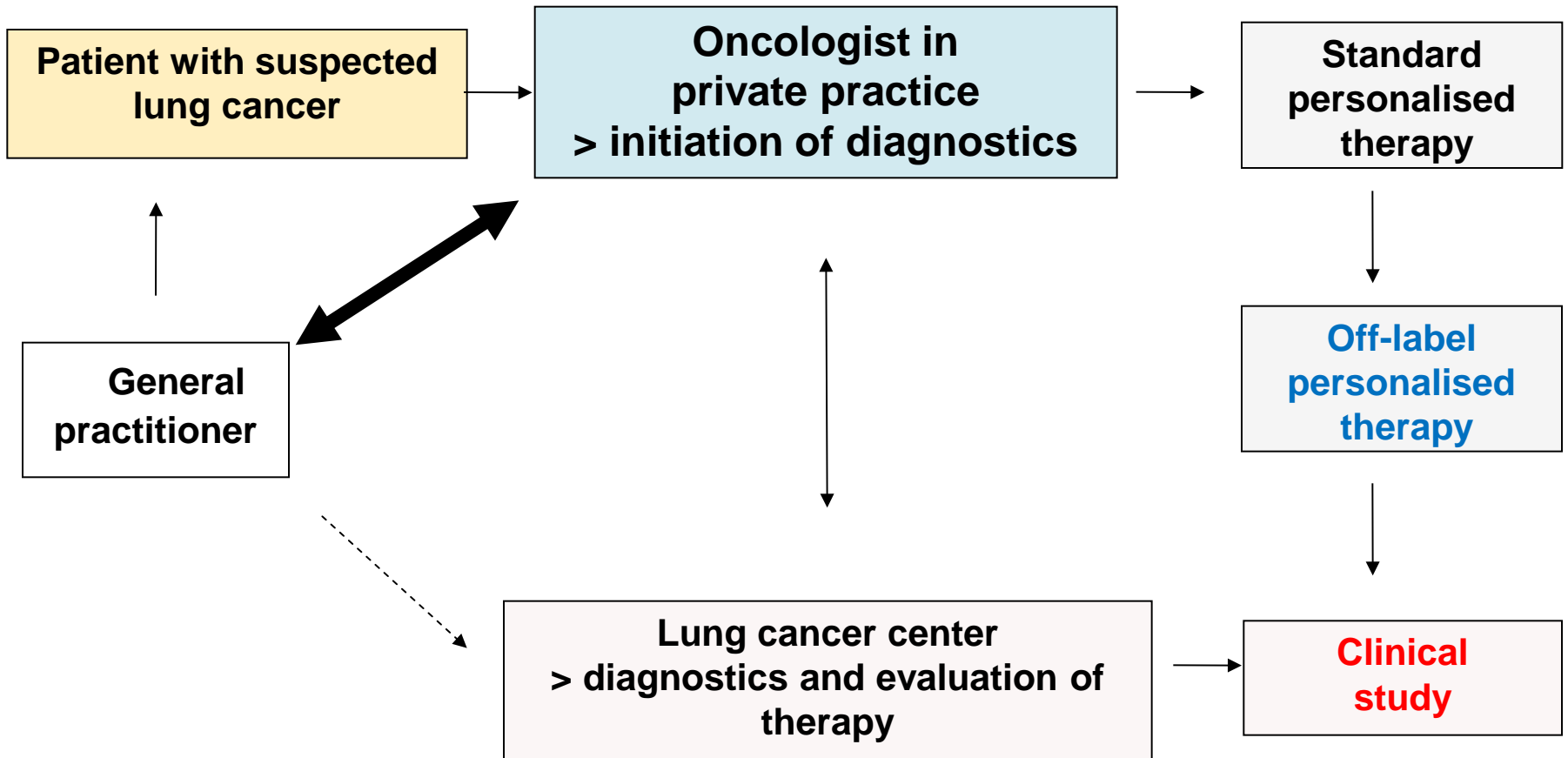
Evaluation of personalized  
therapy:  
- molecular epidemiology  
- outcome  
- costs

Cancer Registry CIO

Cancer Registry NRW

Translational Genomic  
Research

# Local implementation



# What a patient expects from a local oncologist...

---

- **Direct communication and comprehensive information**
- **Accessibility**
- **Reachability (24hrs emergency phone)**
- **Continuity**
- **Treatment in familiar environment**
- **Outpatient treatment**

*but increasingly also:*

- **Information about latest treatment options**
- **Information about molecular testing**
- **Access to innovative treatment**

# **Needs /concerns of an oncologist in private practice**

---

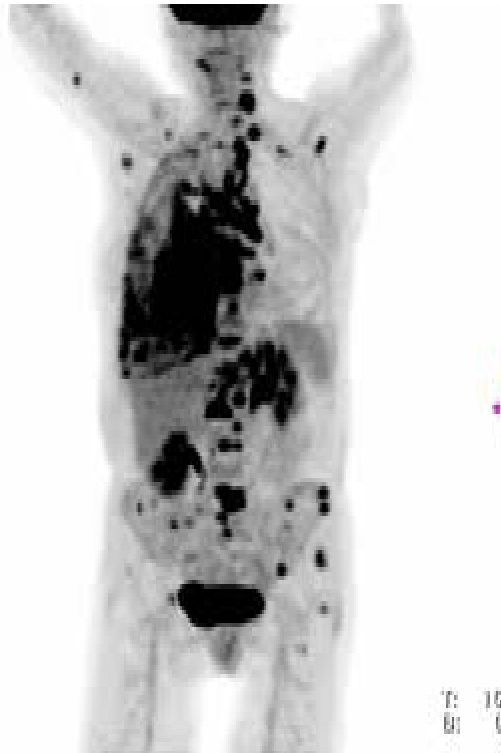
- Collaboration / direct accessibility to lung cancer center**
- Access to clinical studies and new therapies**
- Keeping up-to-date with all the new treatment options**
- Prescription of all approved drugs > exceeding the budget**
- Off-label prescription > fear of penalization**
- Preservation of established structures with respect to collaboration with GPs, local pharmacy, local pathology**

# Patient with ROS1+ lung cancer and progressive disease after chemotherapy: response to ROS1-inhibitor

---



Before therapy



Initiation of  
ROS-1 inhibitor  
treatment



6 weeks later



Network  
Genomic Medicine  
Lung Cancer

## **The Patient´s Perspective**

Bärbel Söhlke, Düsseldorf – Patient





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



A large, light gray graphic of a stylized plant with two leaves and a stem, positioned on the left side of the slide.

# **The payer's perspective**

## Motivation of health insurance company to support nNGM

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Dr. Gerhard Schillinger  
Federal Association of AOK  
(AOK-Bundesverband)

## Motivation of AOK to support nNGM

---

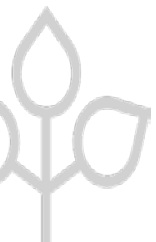
- AOK is an statutory health insurance (AOK=local health insurance fund)
- 11 AOKs, 26,3 million people are insured (32% of the German population )
- payments and reimbursements for medical treatment
- committed to high-quality in medical care



## The German reimbursement system allows for fast introduction of new treatments

---

- reimbursement of all authorised medicinal products – from the day of approval
- new procedures are automatically reimbursed by diagnosis related groups (DRGs) in hospitals
- reimbursement of molecular companion diagnostics in out-patient sector
- But: knowledge-transfer is an issue to be solved



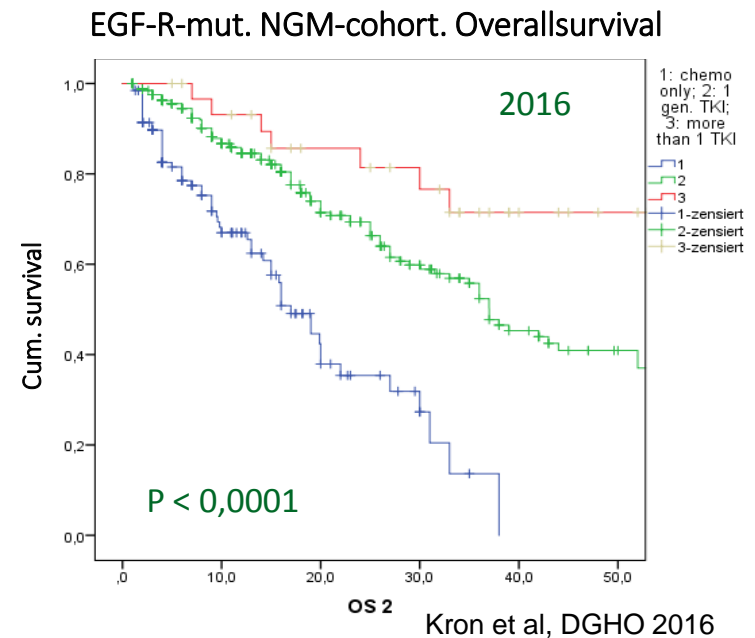
# knowledge-transfer: the time lag between evidence and patient benefit

- 22.000 new cases of advanced NSCLC in 2017 (AOK)
- 9.000 new cases of advanced NSCLC with systemic therapy:

	patients	expected
EGF-R (Gefitinib, Erlotinib, Afatinib, Osimertinib)	344 (3.8%)	5.5% - 10%
ALK, ROS (Crizotinib, Ceritinib)	107 (1.2%)	5.5%
Pembrolizumab (PD1)	895 (9.6%)	20-25% in 2017**
Nivolumab (PD1)*	748 (8.3%)	Off-label use

\* No benefit in POF and OAS compared to chemotherapy in Checkmate026 (first announced 8/2016, ESMO October 9, 2016; Carbone et al., 2017, N Engl J Med 2017; 376:2415-2426)

\*\* 9/2018 EU-approval first-line therapy (+CT) independent of PDL1-Status



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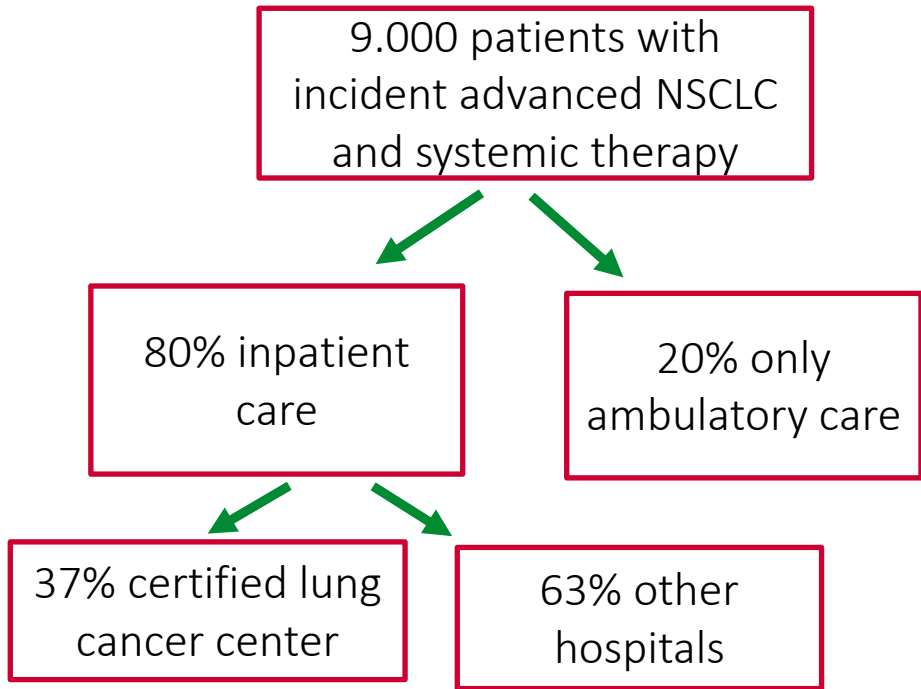
To many patients with molecular changes with proven therapeutic relevance don't get adequate therapy

Up to 60 Million € spending without patient benefit

\* No benefit in POF and OAS compared to chemotherapy in Checkmate026 (first announced 8/2016, ESMO October 9, 2016; Carbone et al., 2017, N Engl J Med 2017; 376:2415-2426)

\*\* 9/2018 EU-approval first-line therapy (+CT) independent of PDL1-Status

# Knowledge-transfer: no higher rates of adequate precision therapy in lung cancer centers



	Lung- Cancer-Centers n=2757	Other hospitals n=4917
EGF-R (Gefitinib, Erlotinib, Afatinib, Osimertinib)	113 (4.1%)	204 (4.2%)
ALK, ROS (Crizotinib, Ceritinib)	29 (1.4%)	63 (1.3%)
Pembrolizumab (PD1)	331 (12%)	517 (10,5%)
Nivolumab (PD1)*	316 (11.5%)	567 (11.6%)

\* off-label use



## Motivation of AOK to support nNGM

---

- structures for high quality cancer treatment are established, funded by the German Cancer Aid
  - patients get reliable and sensitive molecular tumor analysis, clinical relevant mutations will be published
  - direct knowledge-transfer: all patients will get targeted treatment options according to current evidence
  - off-label therapy only in trials or with collection of clinical data
  - patients are treated close to their homes, relatives and friends
  - It works! Cooperation of the AOK RH with NGM since 2014
- ➔ close to home interdisciplinary cancer services of the highest quality for all AOK insured patients with lung cancer



Network  
Genomic Medicine  
Lung Cancer

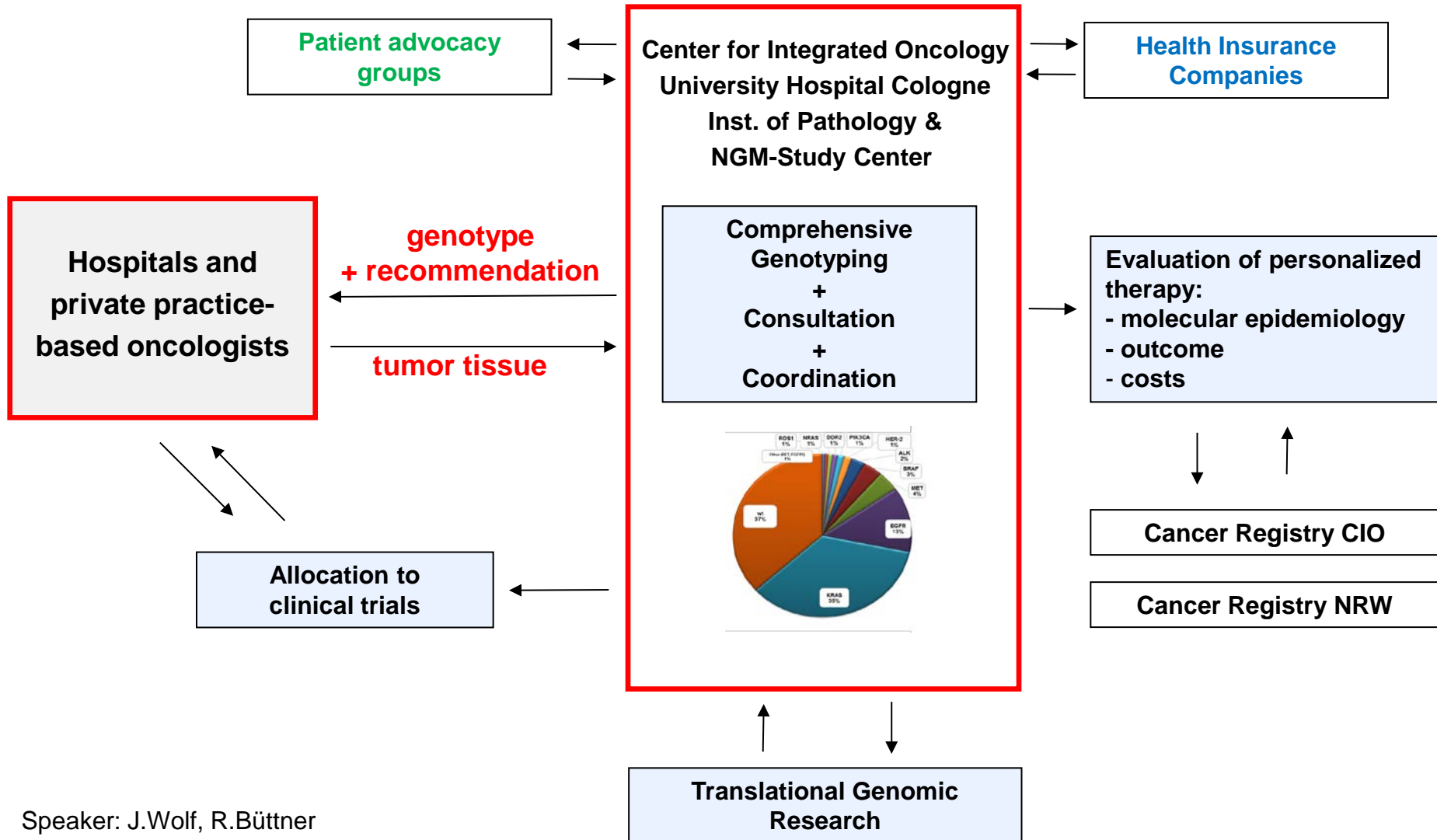
## **Next Steps**

Jürgen Wolf, Cologne – Medical Oncologist



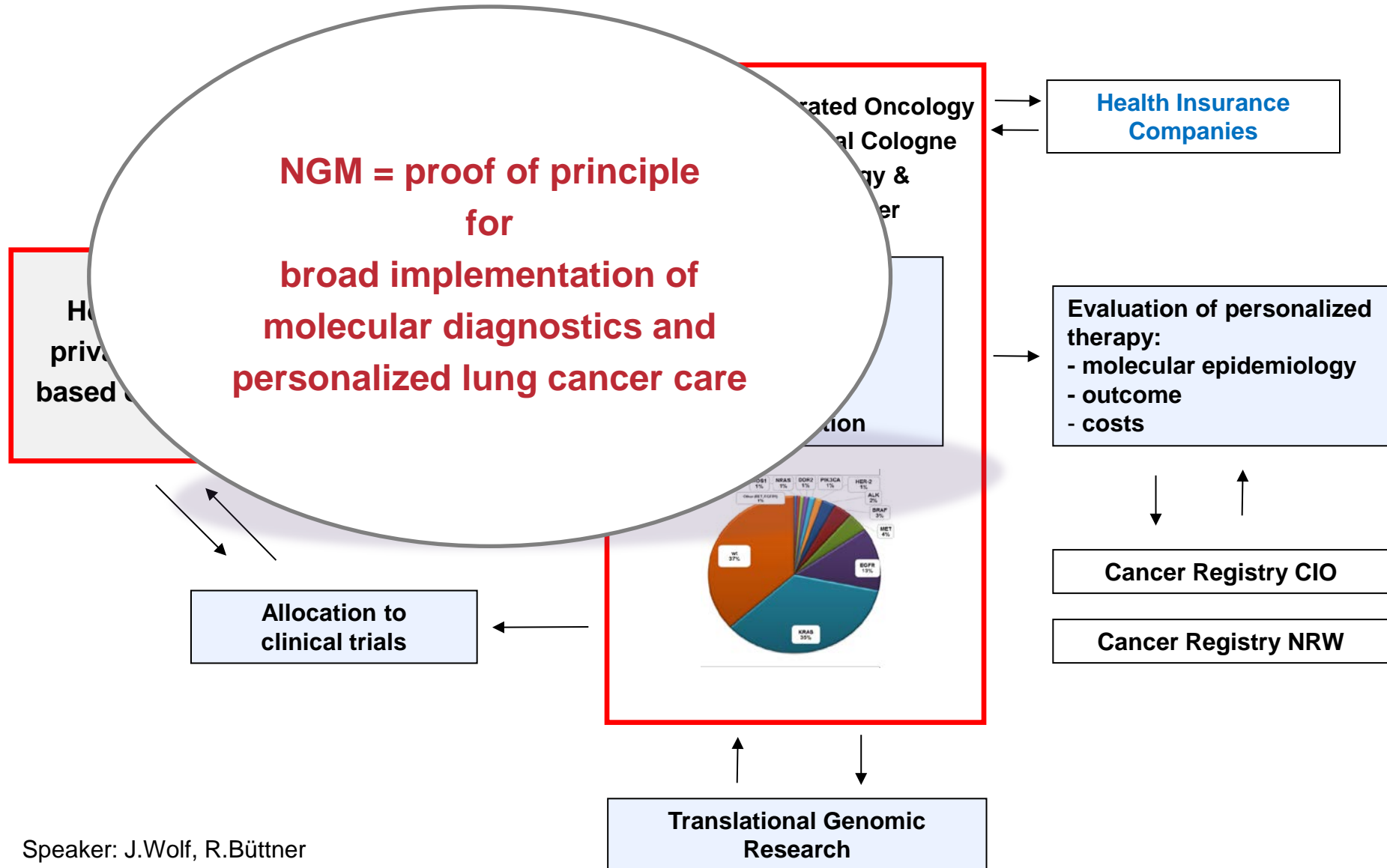
# Network Genomic Medicine:

Founded in 2010 with funding from Ministry for Innovation and Research NRW



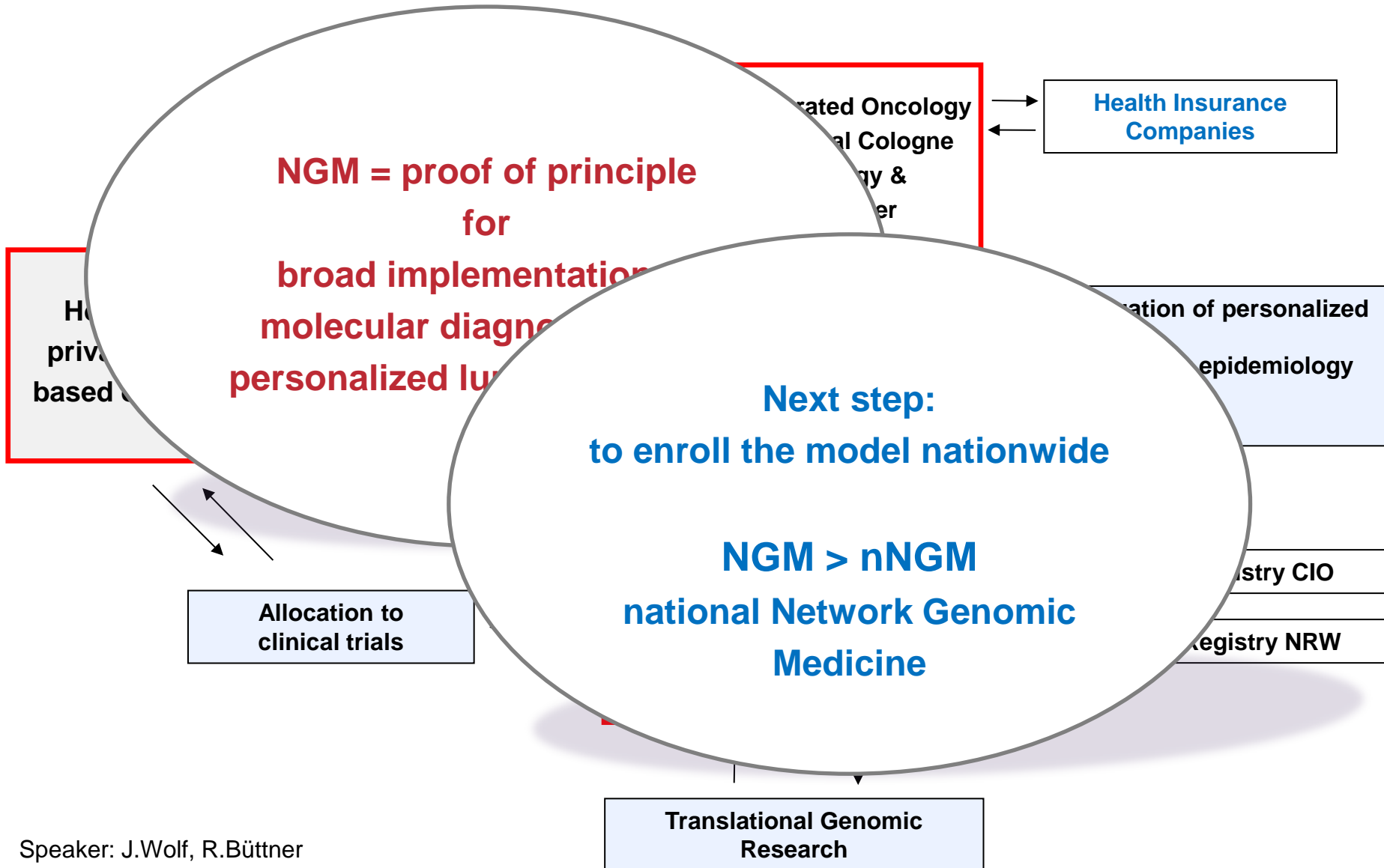
# Network Genomic Medicine:

Founded in 2010 with funding from Ministry for Innovation and Research NRW



# Network Genomic Medicine:

Founded in 2010 with funding from Ministry for Innovation and Research NRW



# national Network Genomic Medicine Lung Cancer

Funding by the German Cancer Aid since 04/18



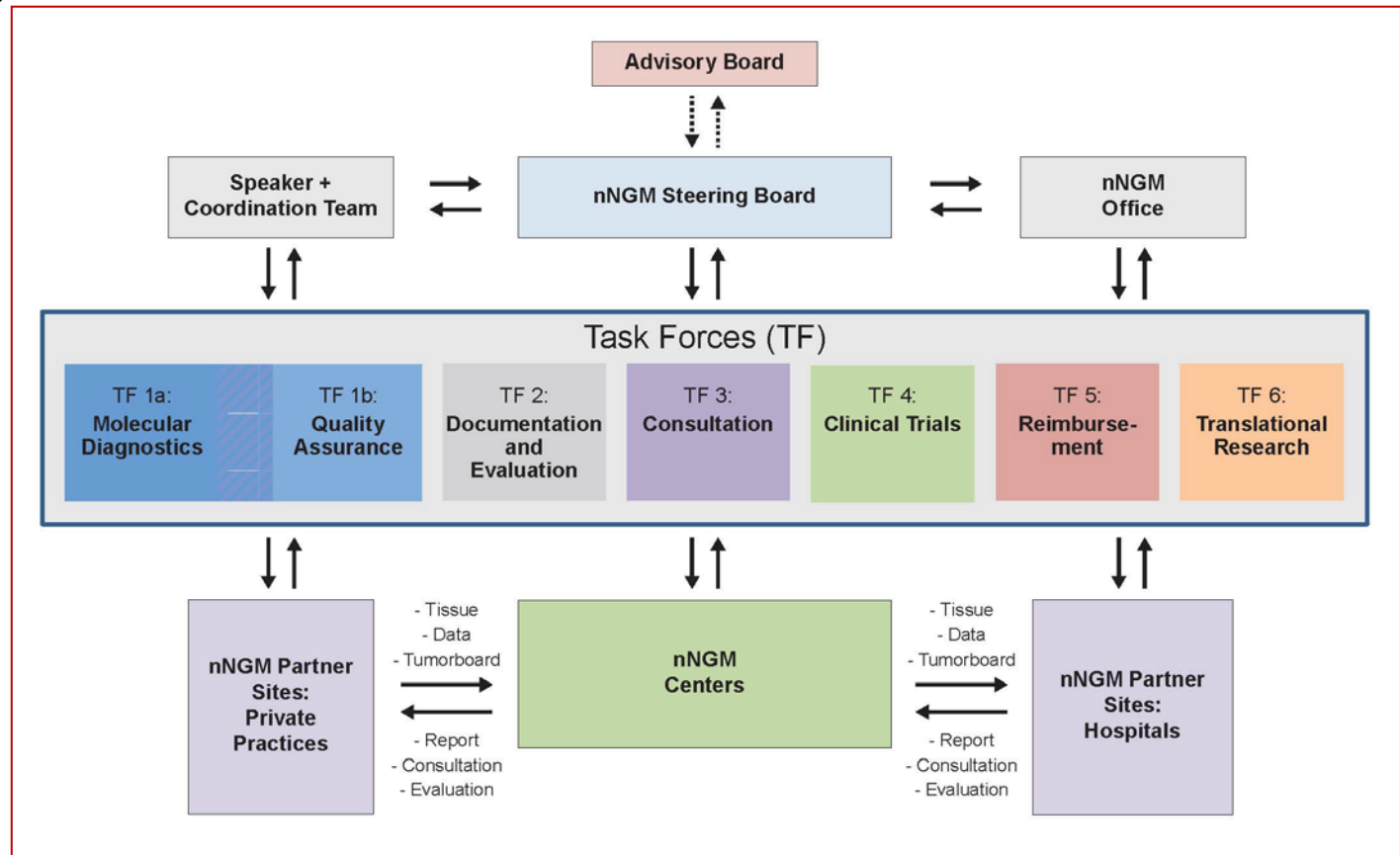
nNGM | National Network  
Genomic Medicine  
Lung Cancer

## 15 German Oncology Centers of Excellence

Berlin  
Dresden  
Düsseldorf  
Erlangen  
Essen  
Frankfurt  
Freiburg  
Hamburg  
Heidelberg  
Köln/Bonn  
Mainz  
München  
Tübingen-Stuttgart  
Ulm  
Würzburg

### Coordination team:

J Wolf (Köln)  
R Büttner (Köln)  
C v Kalle (Heidelberg)



# national Network Genomic Medicine Lung Cancer

Funding by the German Cancer Aid since 04/18



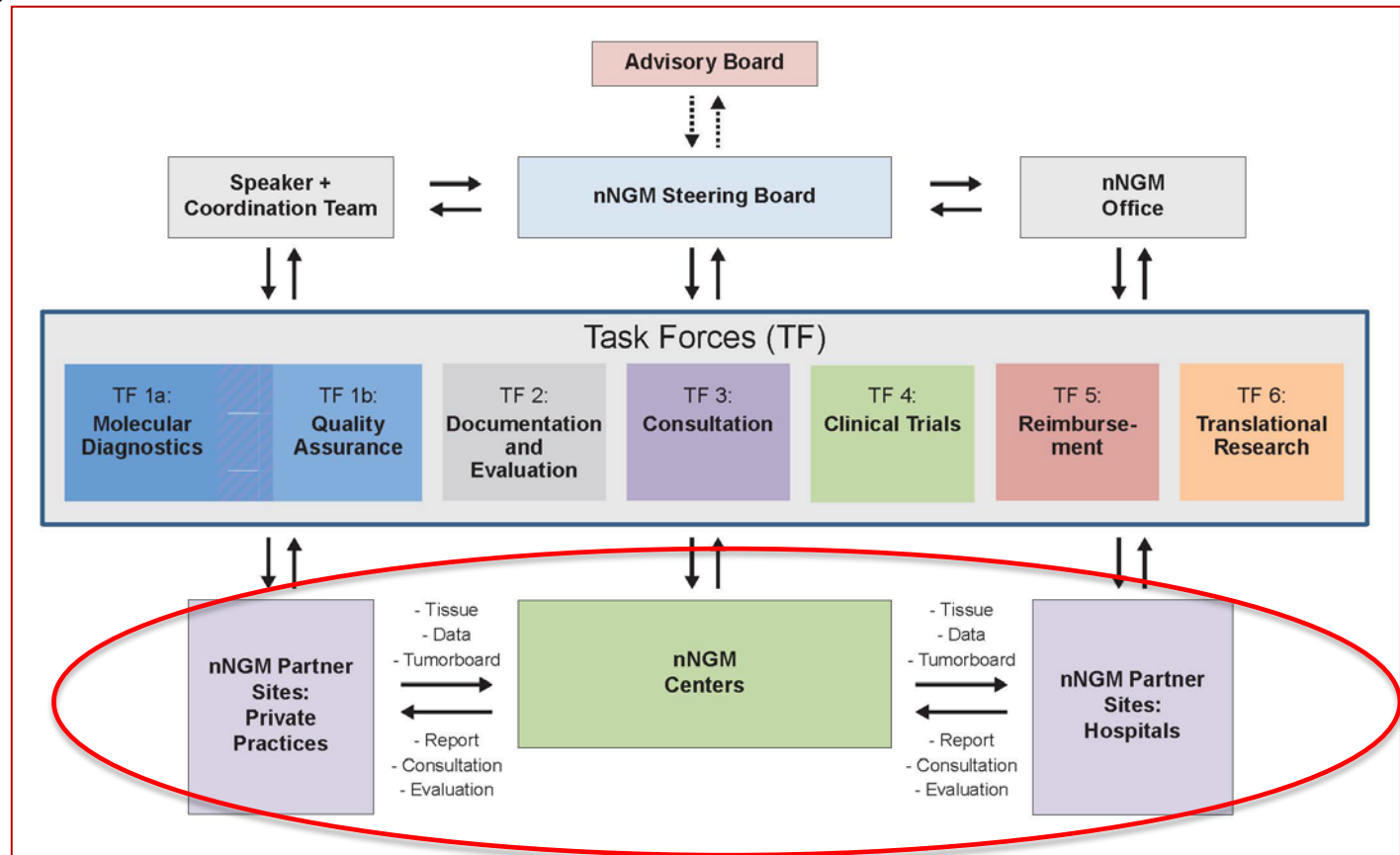
nNGM | National Network  
Genomic Medicine  
Lung Cancer

## 15 German Oncology Centers of Excellence

Berlin  
Dresden  
Düsseldorf  
Erlangen  
Essen  
Frankfurt  
Freiburg  
Hamburg  
Heidelberg  
Köln/Bonn  
Mainz  
München  
Tübingen-Stuttgart  
Ulm  
Würzburg

### Coordination team:

J Wolf (Köln)  
R Büttner (Köln)  
C v Kalle (Heidelberg)



# national Network Genomic Medicine Lung Cancer

Funding by the German Cancer Aid since 04/18



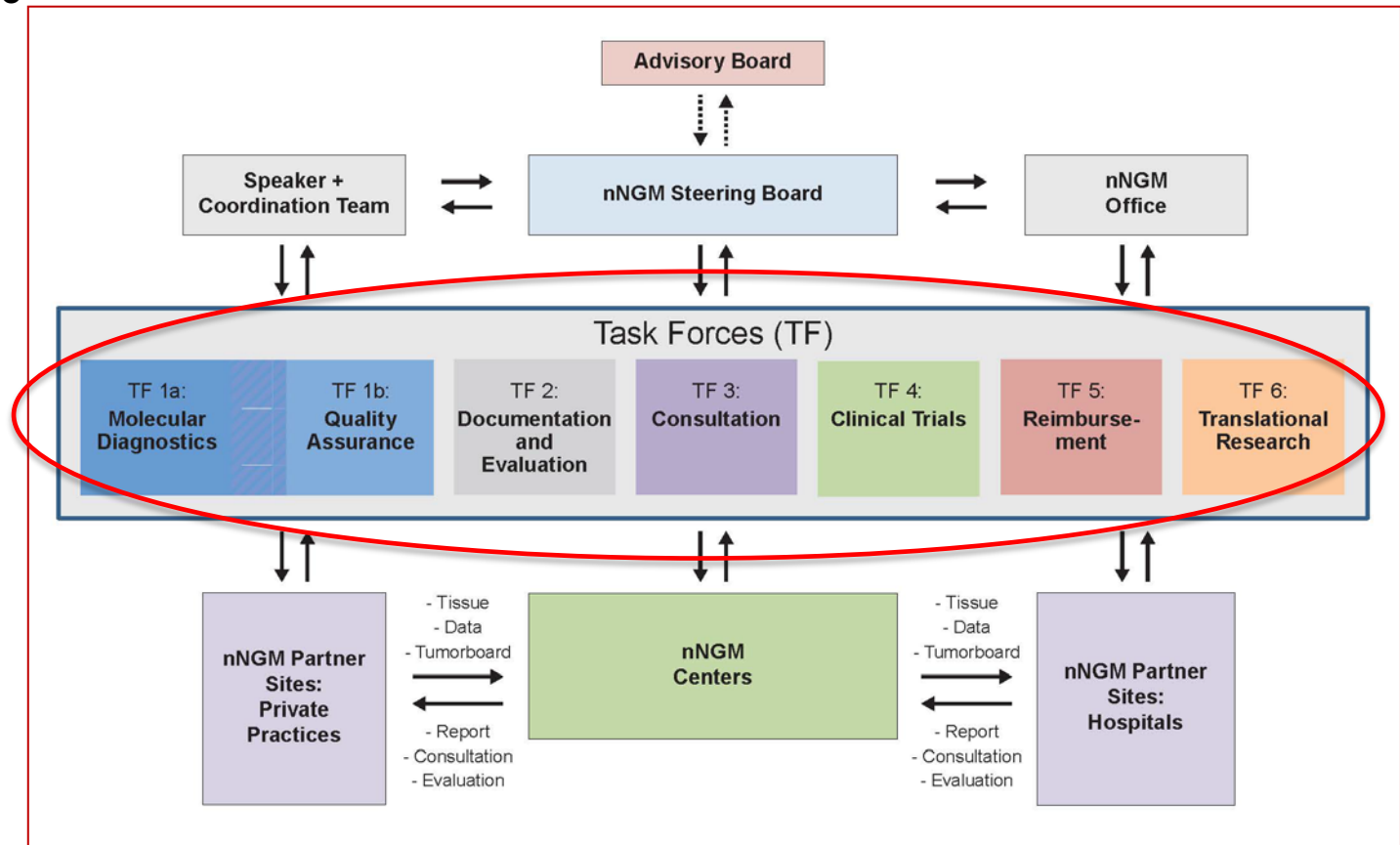
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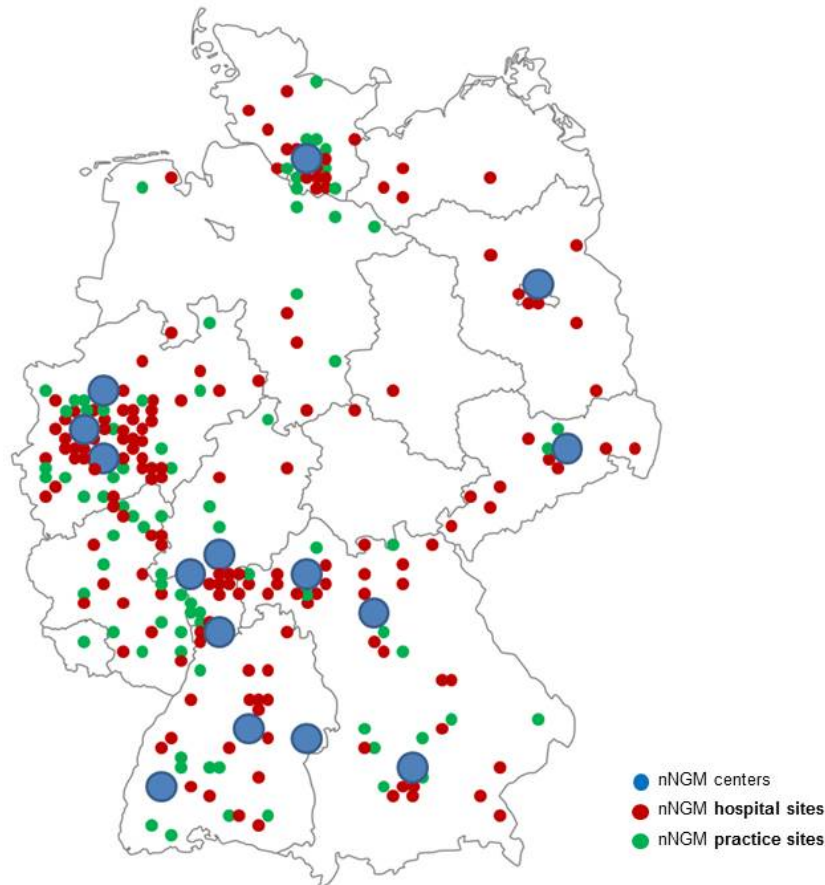


# Development of regional networks



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Current status: regional partners



**2018:**

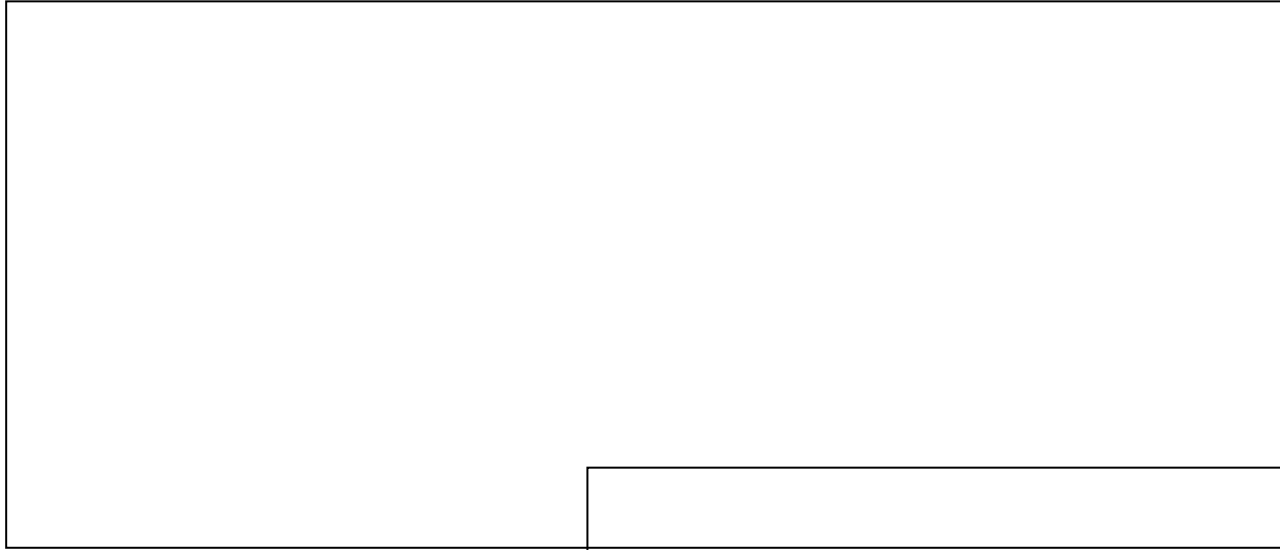
**ca. 10.000 patients  
with advanced lung  
cancer and molecular  
diagnostics**

**> ca. 1/3 of the  
target population**

[www.nngm.de](http://www.nngm.de)



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# Thank you !



nNGM

National Network  
Genomic Medicine  
Lung Cancer

- nNGM centers
- Task Force - speakers
- center managers
- nNGM office team in Cologne

- **all the regional network partners of nNGM and NGM**



Network  
Genomic Medicine  
Lung Cancer

▪ LungCancerGroup  
Cologne

- all the patients and their families

THE **ROSI** DERS  
BRIDGING ROSI+ PATIENTS TO RESEARCH

- Ministry of Culture and Science NRW
- Fed. Ministry of Education and Research
- German Cancer Aid



Bundesministerium  
für Bildung  
und Forschung

Ministerium für  
Kultur und Wissenschaft  
des Landes Nordrhein-Westfalen



- Health Insurance Companies



... and many others health insurances