



nNGM

National Network
Genomic Medicine
Lung Cancer

Implementing personalized lung cancer care in clinical routine: the national Network Genomic Medicine

Jürgen Wolf

Center for Integrated Oncology, University Hospital of Cologne



Network
Genomic Medicine
Lung Cancer

LungCancerGroup
Cologne

CIO Center for
Integrated Oncology
Köln Bonn

Disclosures

- **Advisory boards und lecture fees:**

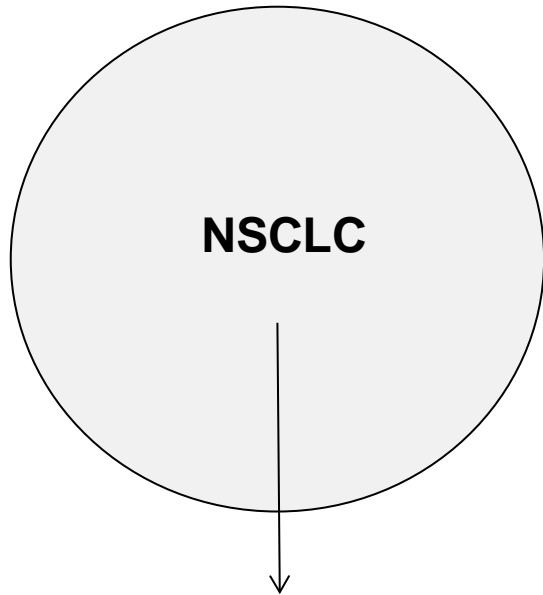
Abbvie, AstraZeneca, BMS, Boehringer-Ingelheim, Chugai, Ignyta, Lilly
MSD, Novartis, Pfizer, Roche

- **Research support:**

BMS, MSD, Novartis, Pfizer

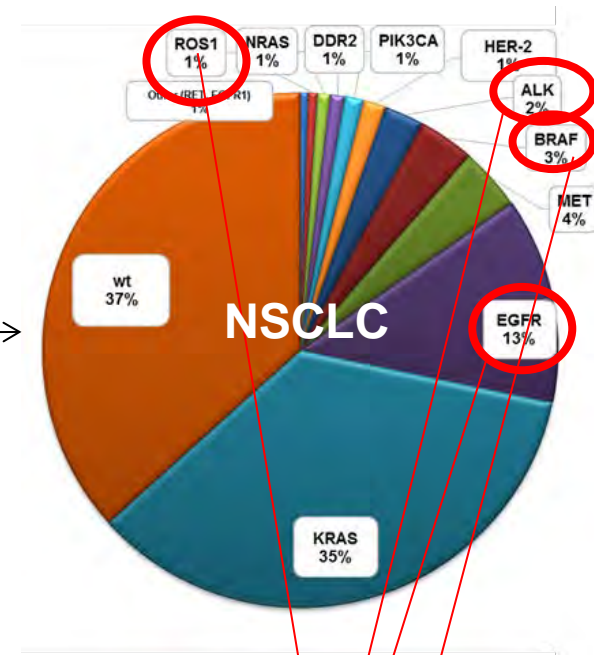
Systemic cancer therapy turns into personalized therapy: example non-small cell lung cancer (NSCLC)

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

Targetable mutations in NSCLC (Jan. 2019)

(without resistance mutations and without markers for immunotherapy)

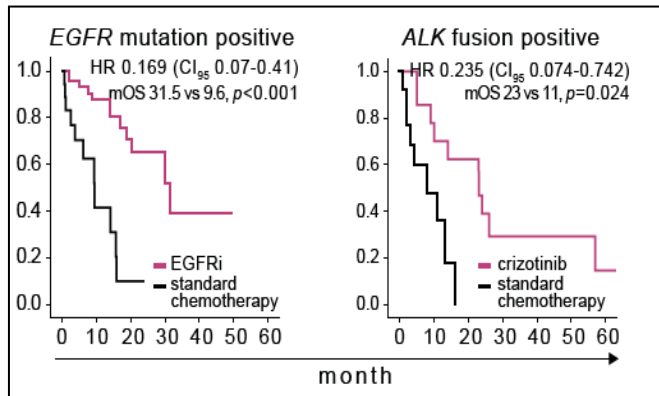
Gene	Alteration	frequency (NSCLC)	drugs
EGFR	actvating mutation (ex 19 del., L858R)	10 %	erlotinib, gefitinib, afatinib, osimertinib
ALK	fusions	3%	crizotinib, alectinib, ceritinib,.....
ROS 1	fusions	1%	crizotinib, (cabozantinib, ponatinib....)
BRAFV600	mutation	2%	dabrafenib + trametinib
MET	amplification (GCN>9)	1%	crizotinib, capmatinib, tepotinib
MET	exon 14 skipping	2%	
MET	fusions	< 1%	
RET	fusions	< 1%	cabozantinib, vandetanib, alectinib, LOXO-292
NRG1	fusions	< 1%	afatinib
HER2	mutation	1-2%	(trastuzumab, pertuzumab)
NTRK 1-3	fusions	< 1% (?)	larotrectinib, entrectinib
EGFR	exon 20 insertion	< 1%	poziotinib
FGFR 1-3	fusions, mutations	1% (each)	erdafinib, BGJ398.....
KRAS	mutation	20%	LTT462 (ERKi.) + LXH254 (panRAFi.)

standard
 off-label, trial
 trial only

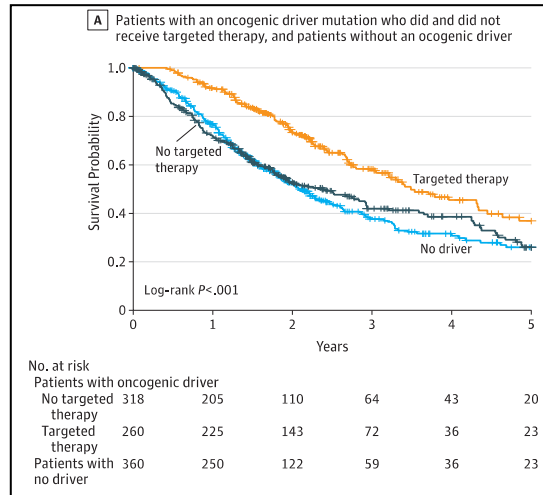
Personalized treatment prolongs survival substantially

Registry data

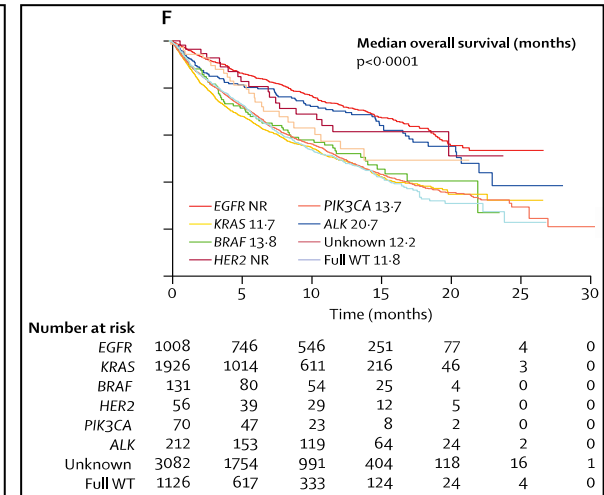
Germany: Network Genomic Medicine



USA: Lung Cancer Mutational Consortium



France: INCA cohort



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

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

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

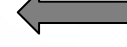
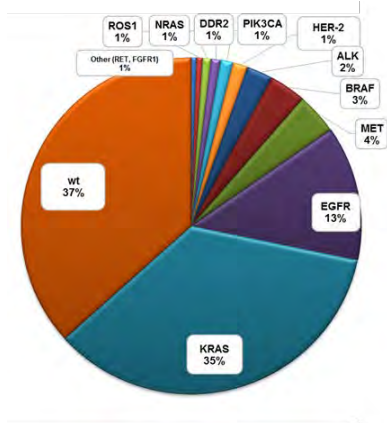
Molecular test rates are not acceptable in Germany

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%)

Lung cancer patients with ROS1 fusion: Molecular testing, off-label treatment and clinical trials save lives



Challenges for the implementation of personalized cancer care into clinical routine

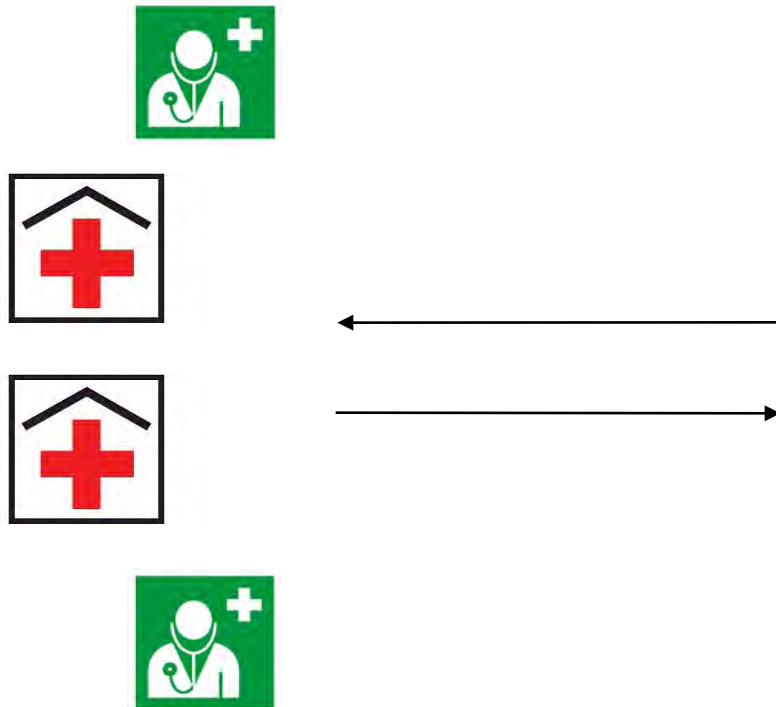


- Implementation of high-quality **molecular multiplex diagnostics**
- State-of-the-art **consultation** with regard to therapeutic consequences
- Rapid **innovation transfer** (new driver mutations) from the academic centers into broad cancer patient care
- **Evaluation** of post-approval and off-label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

Urgent need for building networks

treat close to home

*centralize diagnostics + consultation
+ evaluation*



Oncology Centers of Excellence

- Molecular diagnostics (NGS, WGS, RNA)
- Molecular Tumorboards
- Therapy recommendations
- Translational research
- Databases

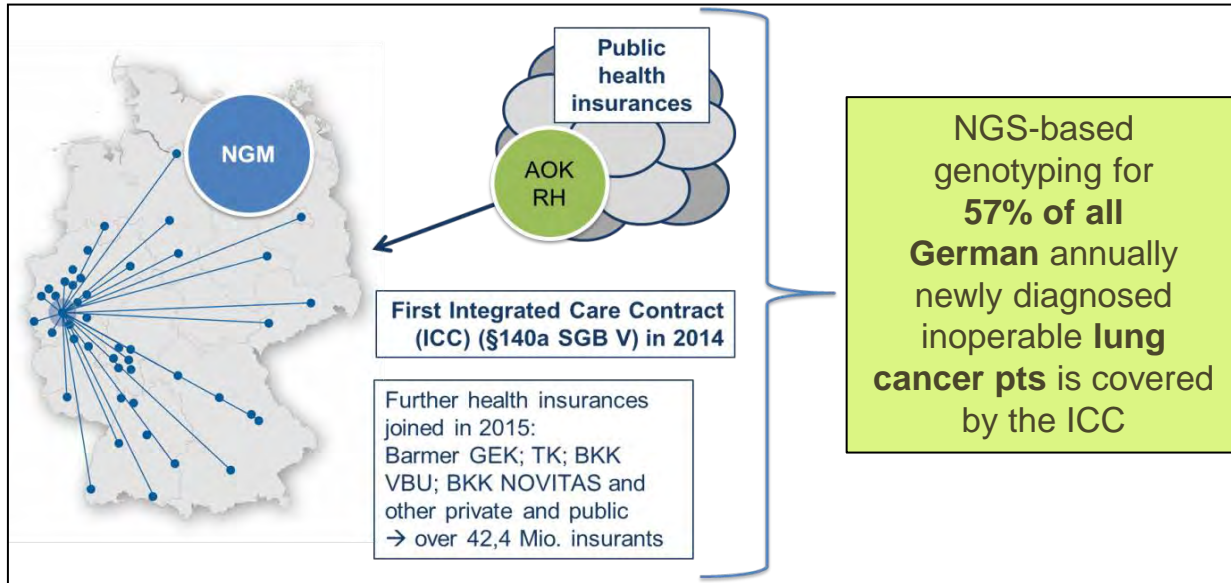
Network Genomic Medicine

founded in 2010 with funding of ministry for innovation NRW
speakers: J.Wolf, R.Büttner; coordinator: A.Kron



Network
Genomic Medicine
Lung Cancer

www.ngm-cancer.com



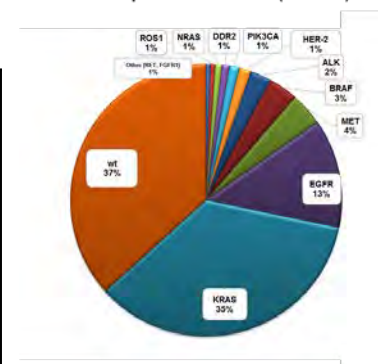
- Centralised NGS-testing of ca. 5000 German lung cancer patients from **ca. 300 referring centers** (ca. 10% of German patients)
- Counseling of referring partners: therapy recommendations
- Clinical trial program with focus on early phase trials
- Cost reimbursement by health insurances (I.V. contract)
- **Central database with ca. 20.000 pts. with genomic and clinical annotation**

> proof of principle for implementation of personalized care

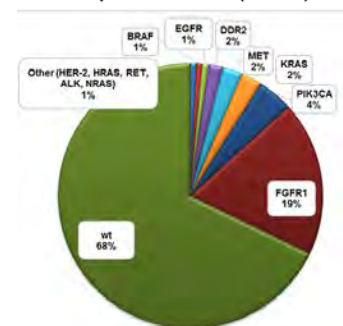
NGM-associated personalized clinical trial program

<p>Phase I/II platform (pharma trials)</p>	<p>EGFR (3rd gen.) mono and combos, FIM ALK (2nd gen.), FIM METamp, METex.14, phase II ROS1, phase I NTRK, BRAF, KRAS, FIM FGFRamp, FIM DLL3 (SCLC), phase II RETfus, phase II</p>
<p>Investigator-initiated trials</p>	<p>EGFR+MEK (EATON), phase I ROS 1 (EUCROSS), phase II HER2mut (TRY), phase II FGFRfus+mut (FIND), phase II TMB (I-O; BIOLUMA), phase II</p>

Non-Squamous NSCLC (n=4244)



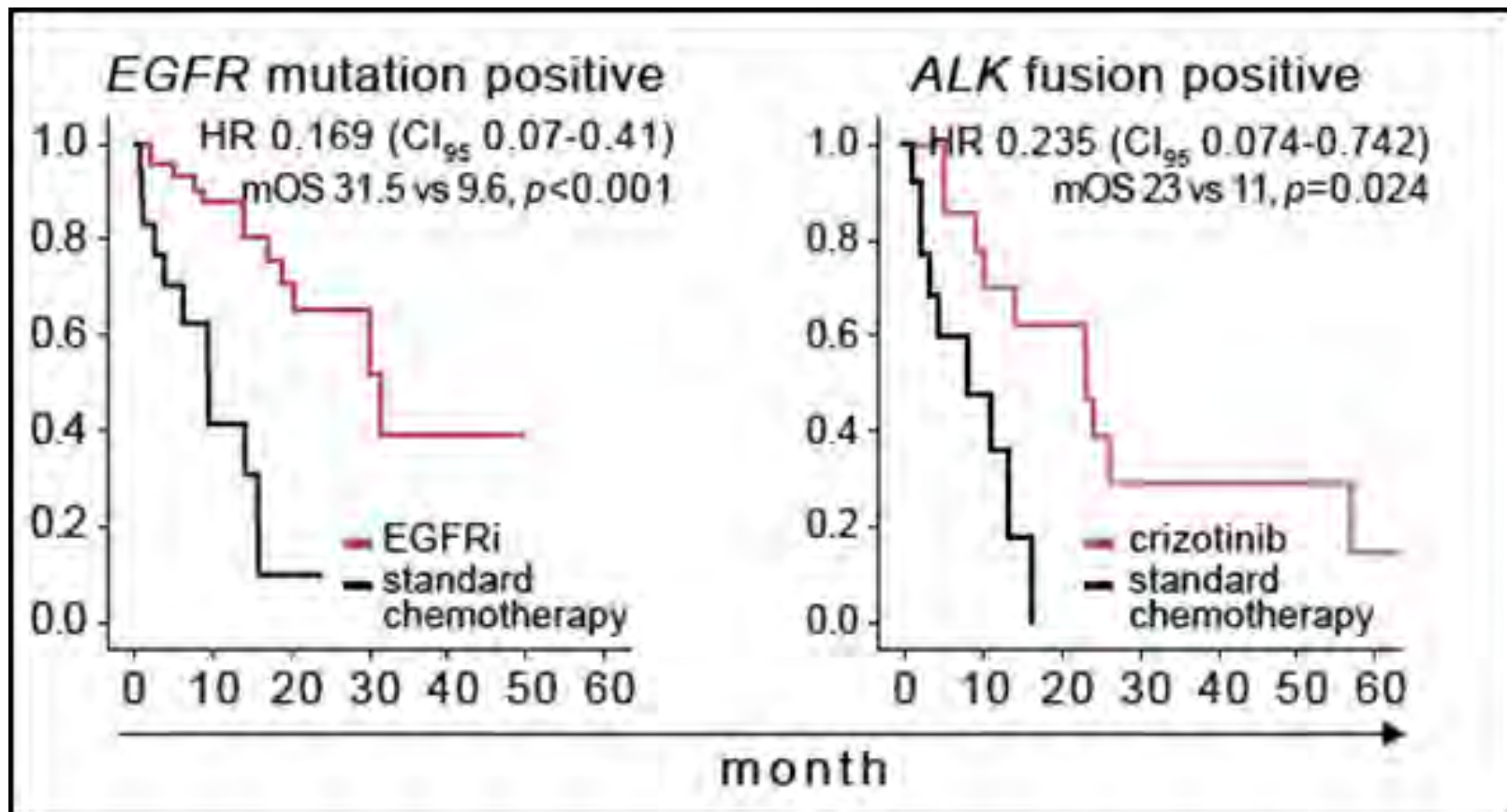
Squamous NSCLC (n=1498)



- > to treat all patients according to the genetic vulnerability of her/his tumor
- > to allow patients early access to innovative drugs
- > to allow proof-of-concept
- > to develop new treatment approaches for small genetic subgroups

1st NGM Evaluation 2013:

Strong OS benefit with personalized therapies





Nationwide extension of the NGM-model

> national Network Genomic Medicine

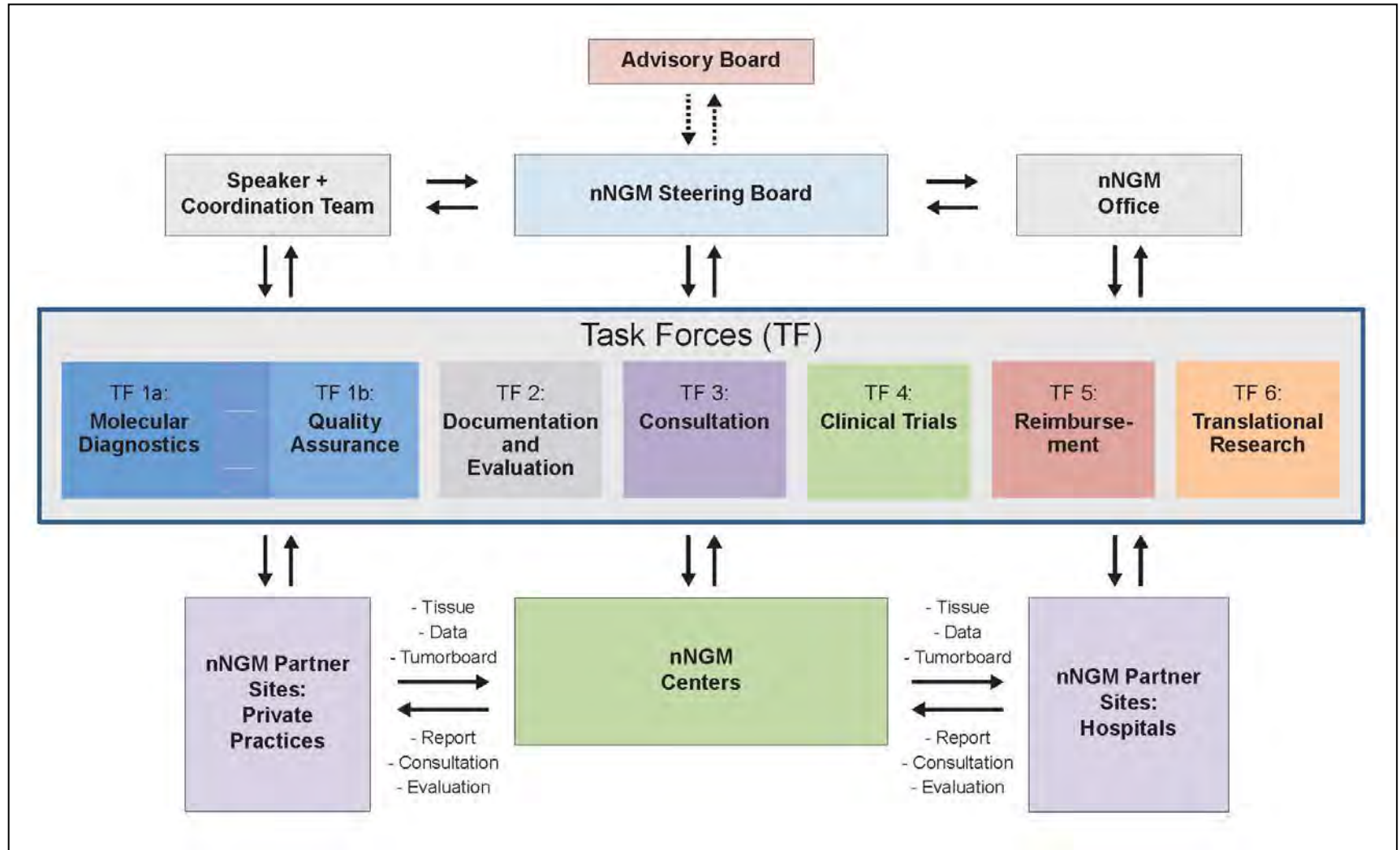
- 10 / 16 Grant application to German Cancer Aid (DKH)
- **04 / 18 Start funding of nNGM by DKH**

Initial nNGM centers = 15 DKH-funded Oncology Centers of Excellence (CCCs):

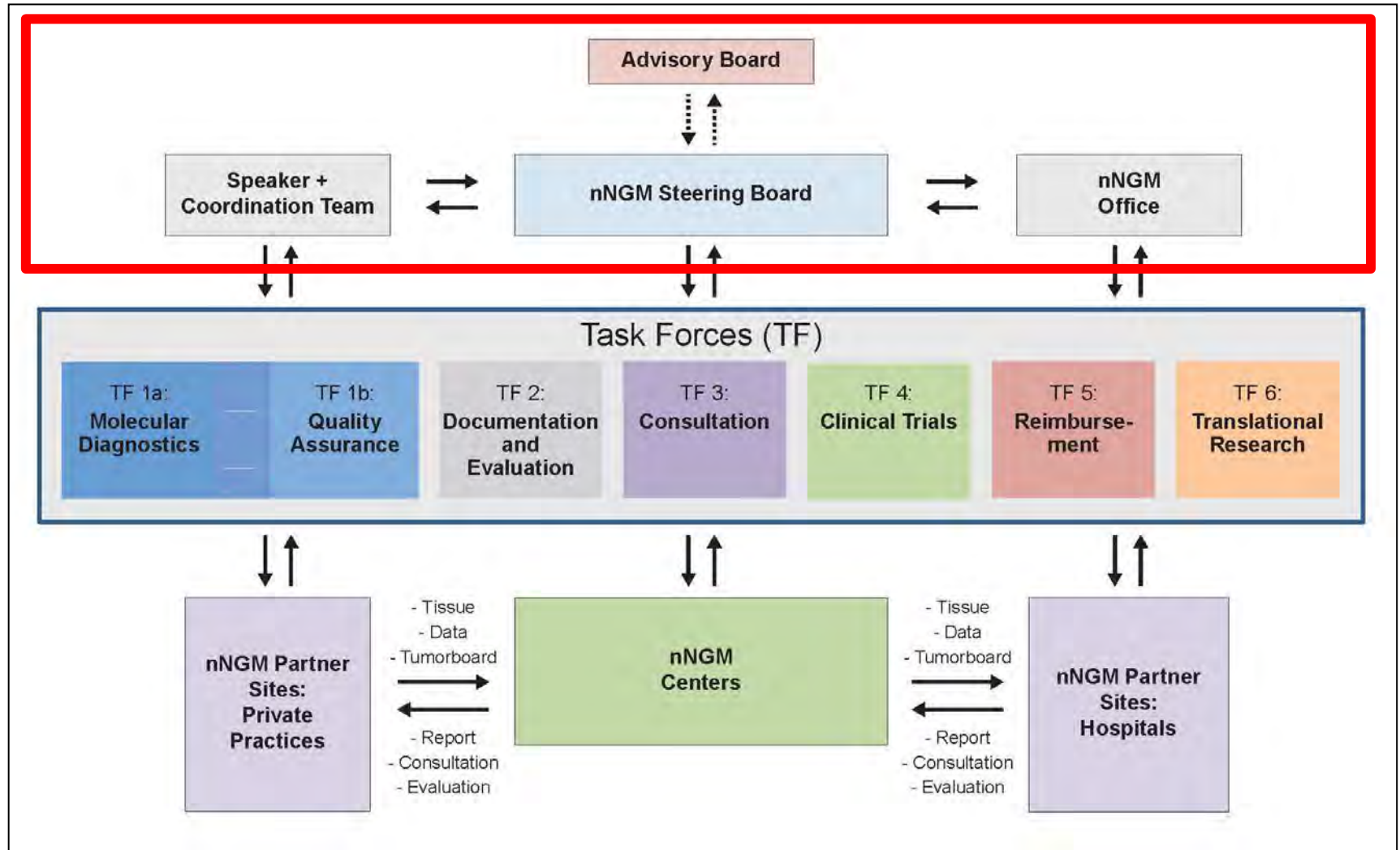
Berlin, Dresden, Düsseldorf, Erlangen, Essen, Frankfurt, Freiburg, Hamburg, Heidelberg, Köln/Bonn, Mainz, München (LMU/TU), Tübingen-Stuttgart, Ulm, Würzburg

- 11 / 18 1st positive evaluation by DKH reviewers

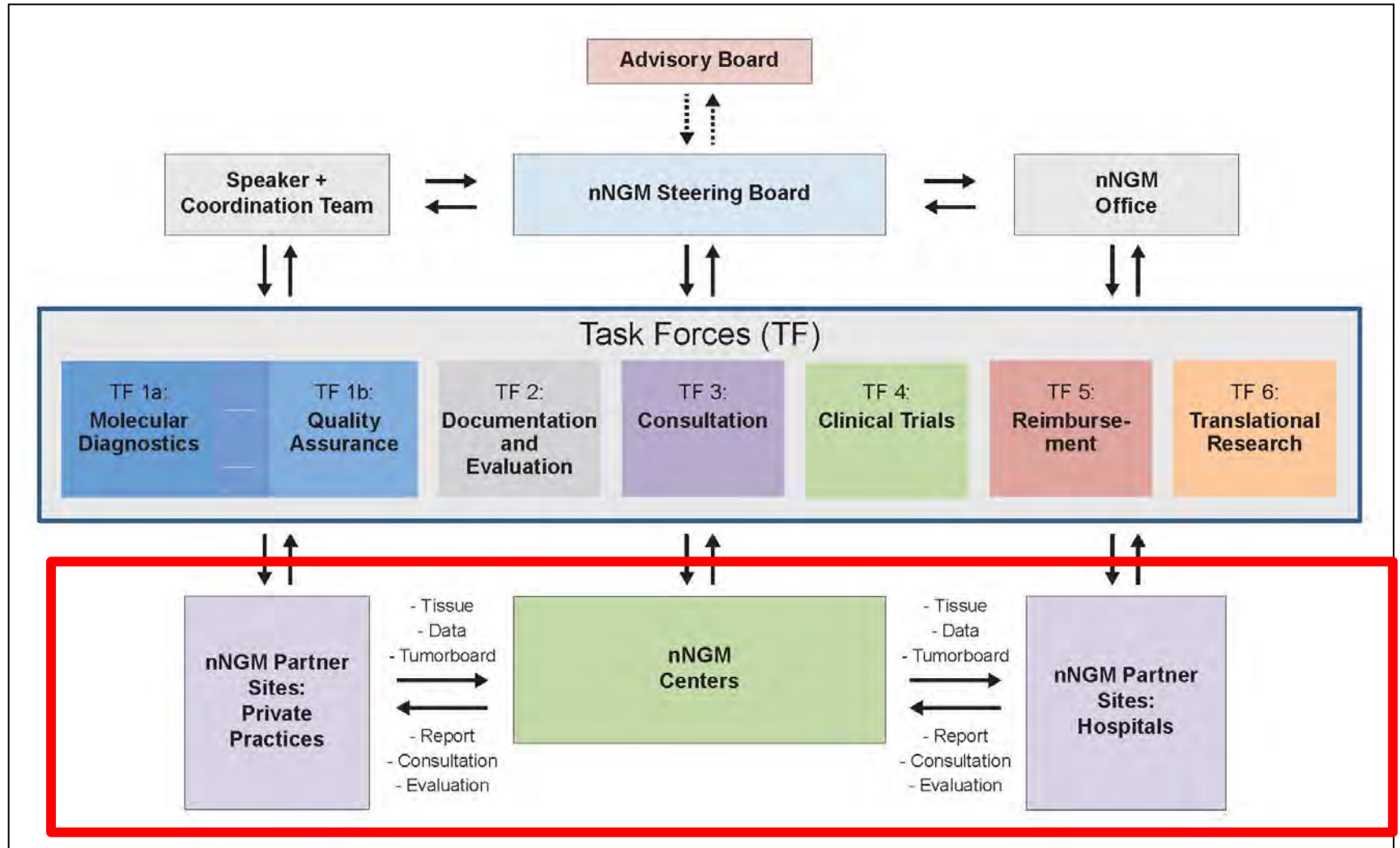
Structure of nNGM: governance, task forces, regional networks



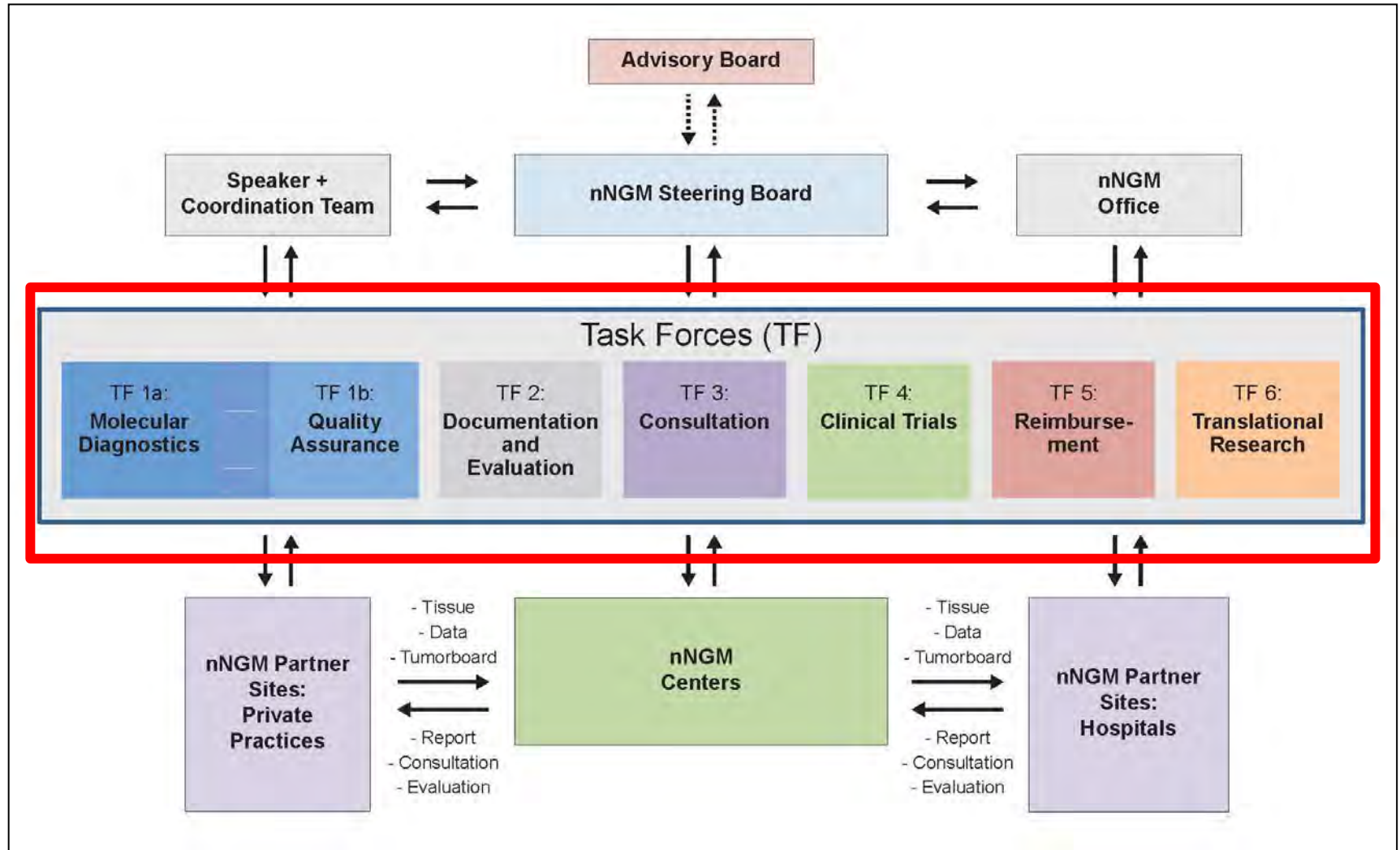
Structure of nNGM: governance, task forces, regional networks



Structure of nNGM: governance, task forces, regional networks



Structure of nNGM: governance, task forces, regional networks



TF 1a: Molecular Diagnostics

Speakers: R. Büttner, F. Haller, S. Merkelbach-Bruse

- **Joint NGS Panel**
- **Joint SOPs for mol. diagnostics NGS, FISH....**
- **Harmonized Reports**
- > **Hybrid-capture based NGS under development**
- > **TMB diagnostics under development**

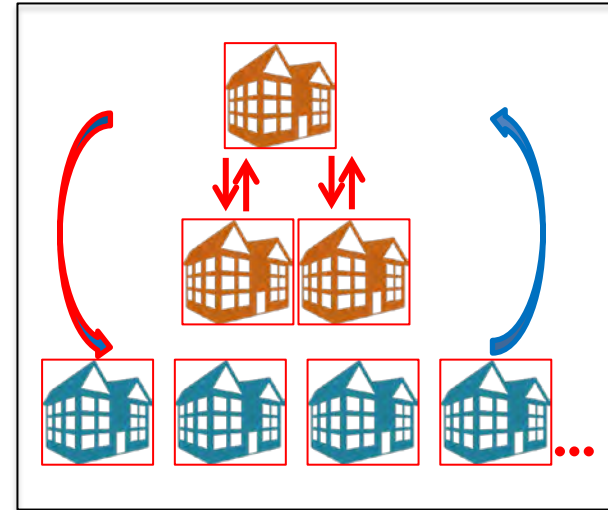
Marker	Transkript	Exone
ALK	NM_004304	22, 23, 24, 25
BRAF	NM_004333	11, 15
CTNNB1	NM_001904	3
EGFR	NM_005228	18, 19, 20, 21
ERBB2 (HER2)	NM_004448	8, 19, 20
FGFR1	NM_023110	4, 5, 6, 7, 10, 12, 13, 14, 15
FGFR2	NM_000141	Tr-A*: 6, 7, 8, 10, 11, 13, 14, 15; Tr-B*: 8, 9, 12, 18
FGFR3	NM_000142	3, 6, 7, 9, 10, 12, 14, 16, 18
FGFR4	NM_213647	3, 6, 9, 12, 13, 15, 16
IDH1	NM_005896	4
IDH2	NM_002168	4
KRAS	NM_033360	2, 3, 4
MAP2K1 (MEK1)	NM_002755	2, 3
MET	NM_001127500	14, 16, 17, 18, 19
MET	NM_001127500	Intron 13, ersten 100 bp von Intron 14
NRAS	NM_002524	2, 3, 4
PIK3CA	NM_006218	10, 21
PTEN	NM_000314	1, 2, 3, 4, 5, 6, 7, 8
ROS1	NM_000245	34, 35, 36, 37, 38, 39, 40, 41
TP53	NM_000546	4, 5, 6, 7, 8

TF 1b: QA Molecular Diagnostics

Speakers: P. Schirmacher, T. Kirchner, M.Hummel

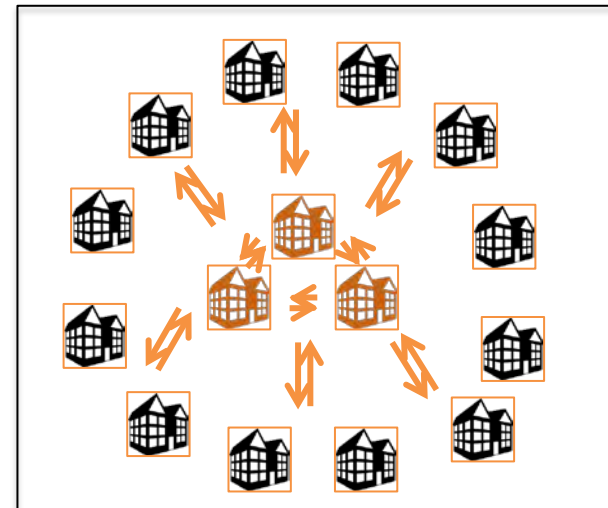
NGS Proficiency Testing

1. Samples tested and retested by reference centers
2. Test and reporting by all centers



NGS Performance Testing

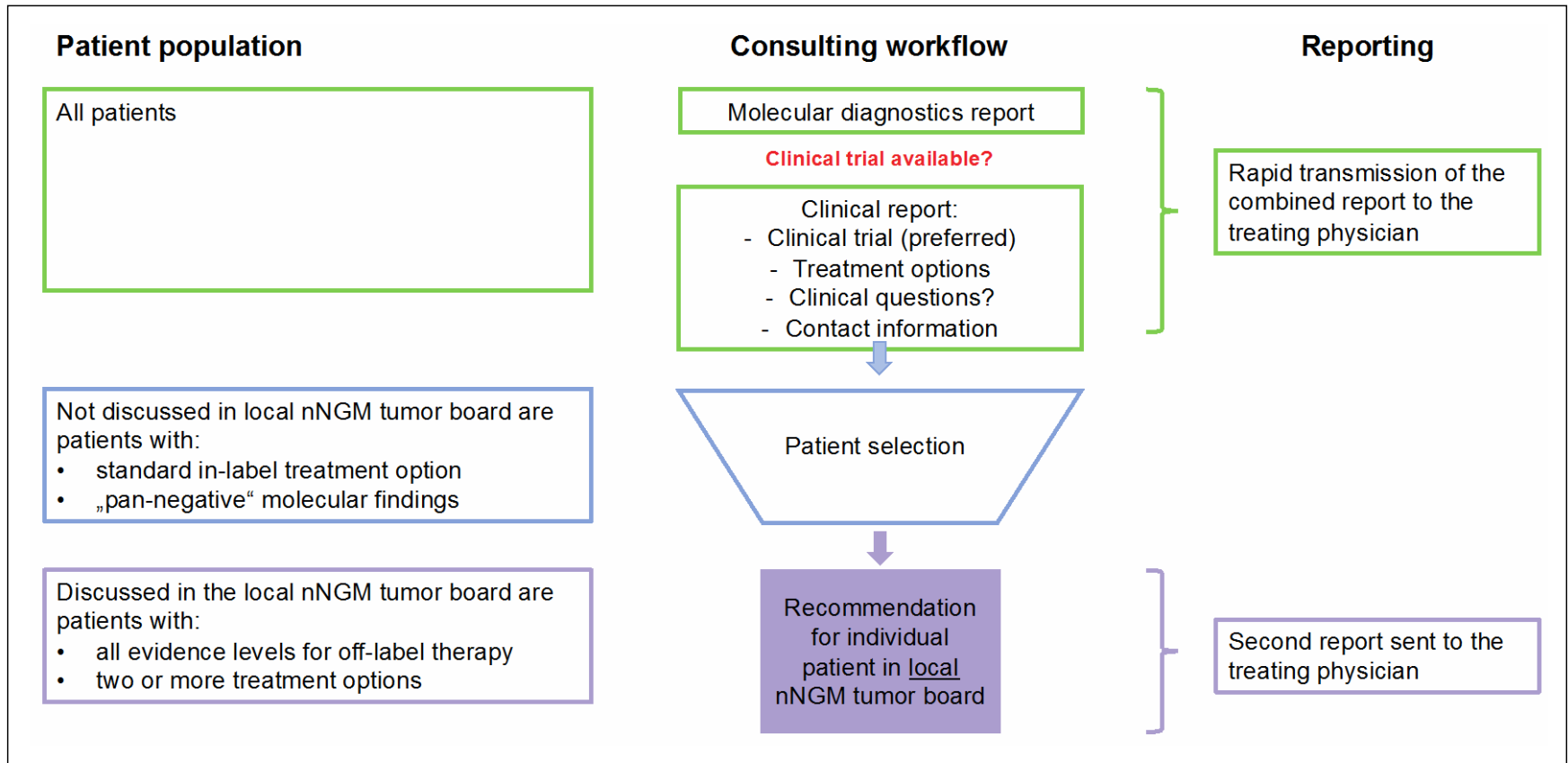
1. Random sample identification in nNGM centers
2. Retesting by reference centers



TF 3: Consultation > harmonized workflow

Speakers: C.Brandts, E.Schröck, N.v.Bubnoff

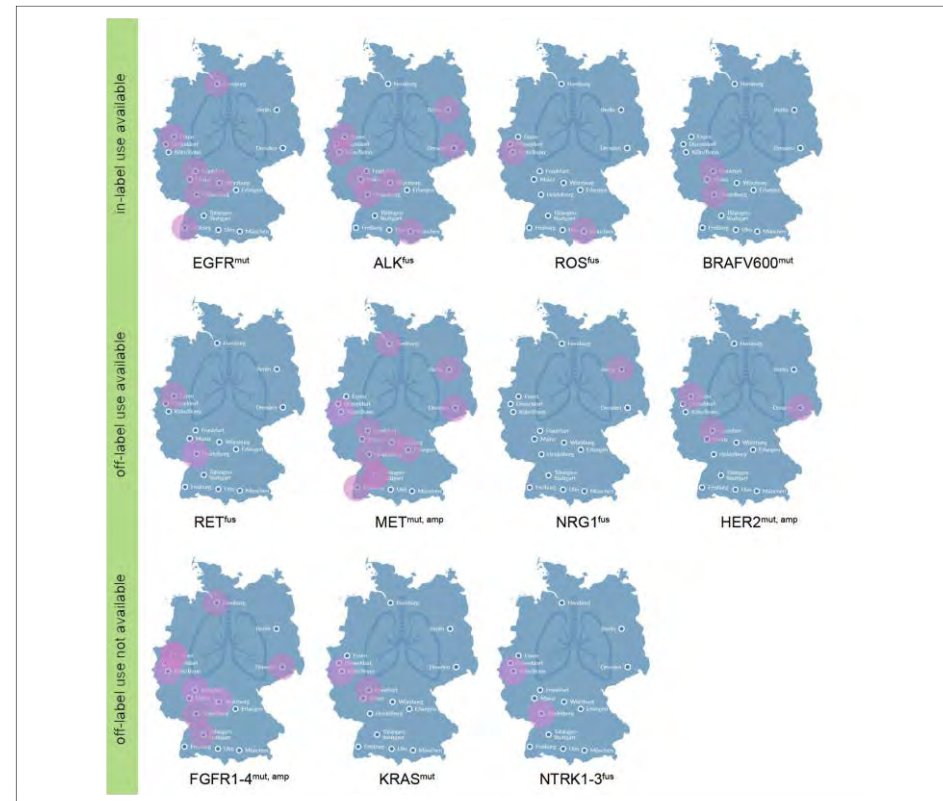
in collaboration with A. Heyll, MDK Kompetenzzentrum Onkologie



TF 4: Clinical Trials

Speakers: J.Wolf, M.Sebastian, M.Thomas

- **Status quo assessment of trial activity in nNGM centers**
> harmonization
- **Central Clinical Trial Registry in collaboration with DKTK**
> www.nngm.de
- **1st nNGM trial launched in Q1 2019: FGFR-inhibition in squamous cell lung cancer (phase II IIT FIND)**





DIE ZENTREN

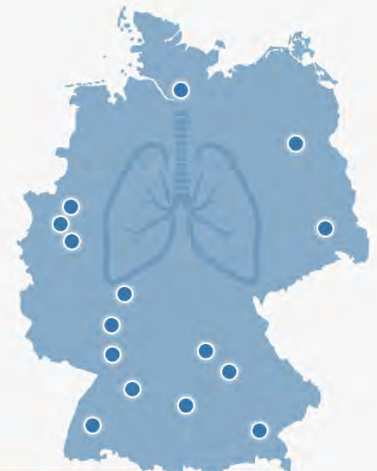
Die Deutsche Krebshilfe fördert 15 universitäre Krebszentren

Über ein bundesweites Netzwerk sollen in Deutschland künftig alle Patienten mit fortgeschrittenem Lungenkrebs Zugang zu molekularer Diagnostik und innovativen Therapien erhalten.

Dafür schließen sich 15 universitäre Krebszentren im „nationalen Netzwerk Genomische Medizin (nNGM) Lungenkrebs“ zusammen – darunter alle 13 onkologischen Spitzenzentren, die aktuell von der Deutschen Krebshilfe gefördert werden.

nNGM ist eine Weiterentwicklung des Kölner Netzwerks Genomische Medizin ([zur Website](#)), das sich seit 2010 erfolgreich für die Implementierung personalisierter Therapien in der Routineversorgung von Patienten mit Lungenkrebs einsetzt. Ziel des bundesweiten Netzwerks ist, den schwerkranken Patienten Zugang zu modernster molekularer Diagnostik und neuesten Therapien, auch im Rahmen klinischer Studien, zu ermöglichen.

Die Deutsche Krebshilfe unterstützt dieses Verbundprojekt seit dem 1. April 2018.



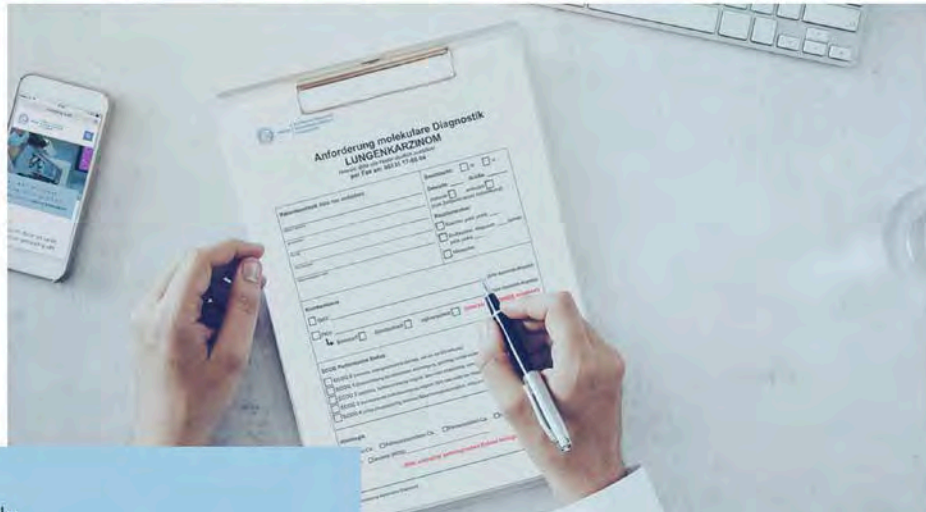
BERLIN	ESSEN	HEIDELBERG	TÜBINGEN-
DRESDEN	FRANKFURT	KÖLN/BOHN	STUTTGART
DÜSSELDORF	FREIBURG	MAINZ	ULM
ERLANGEN	HAMBURG	MÜNCHEN	WÜRZBURG

DIE ZIELE DES

nNGM Verbunds



Aufbau einer gemeinsamen Dokumentations- und



Downloads

ANFORDERUNG

Für Zuweiser:
Anforderungscheine molekulare
Diagnostik Lungenkarzinom

DRESDEN PDF	DÜSSELDORF PDF	ERLANGEN PDF
ESSEN PDF	FRANKFURT PDF	KÖLN Zur Website
BONN PDF	MAINZ PDF	MÜNCHEN LMU+TUM PDF
TÜBINGEN-STUTTGART PDF	WÜRZBURG PDF	ULM PDF

Download:
Test requests for
all nNGM centers

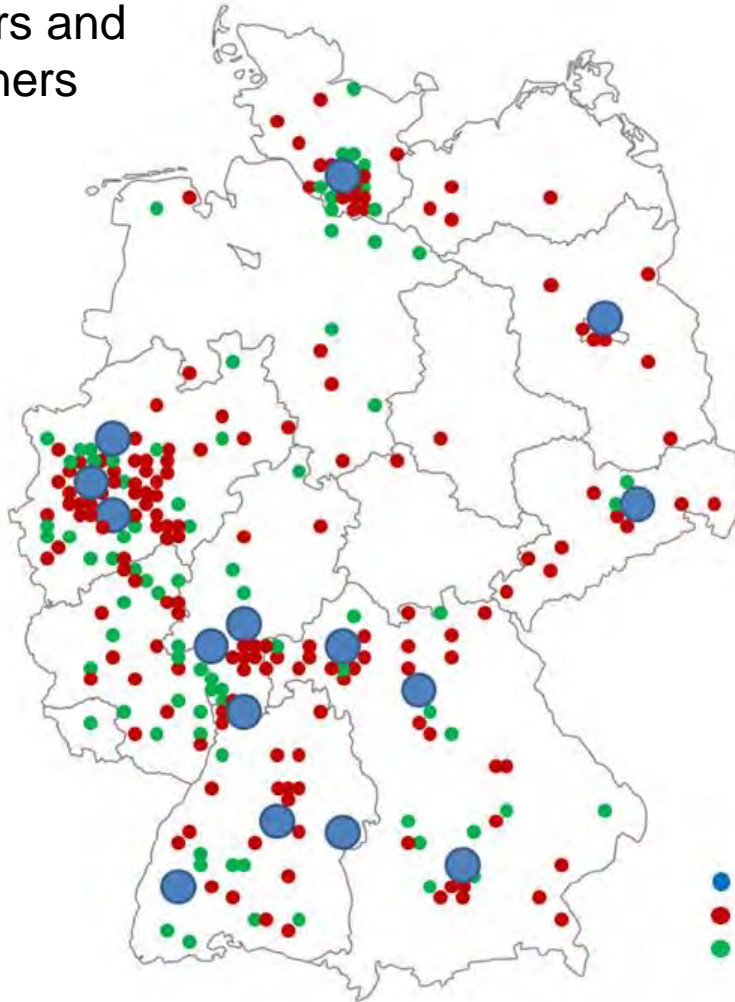
Current status of nNGM



nNGM

National Network
Genomic Medicine
Lung Cancer

nNGM-centers and
network partners



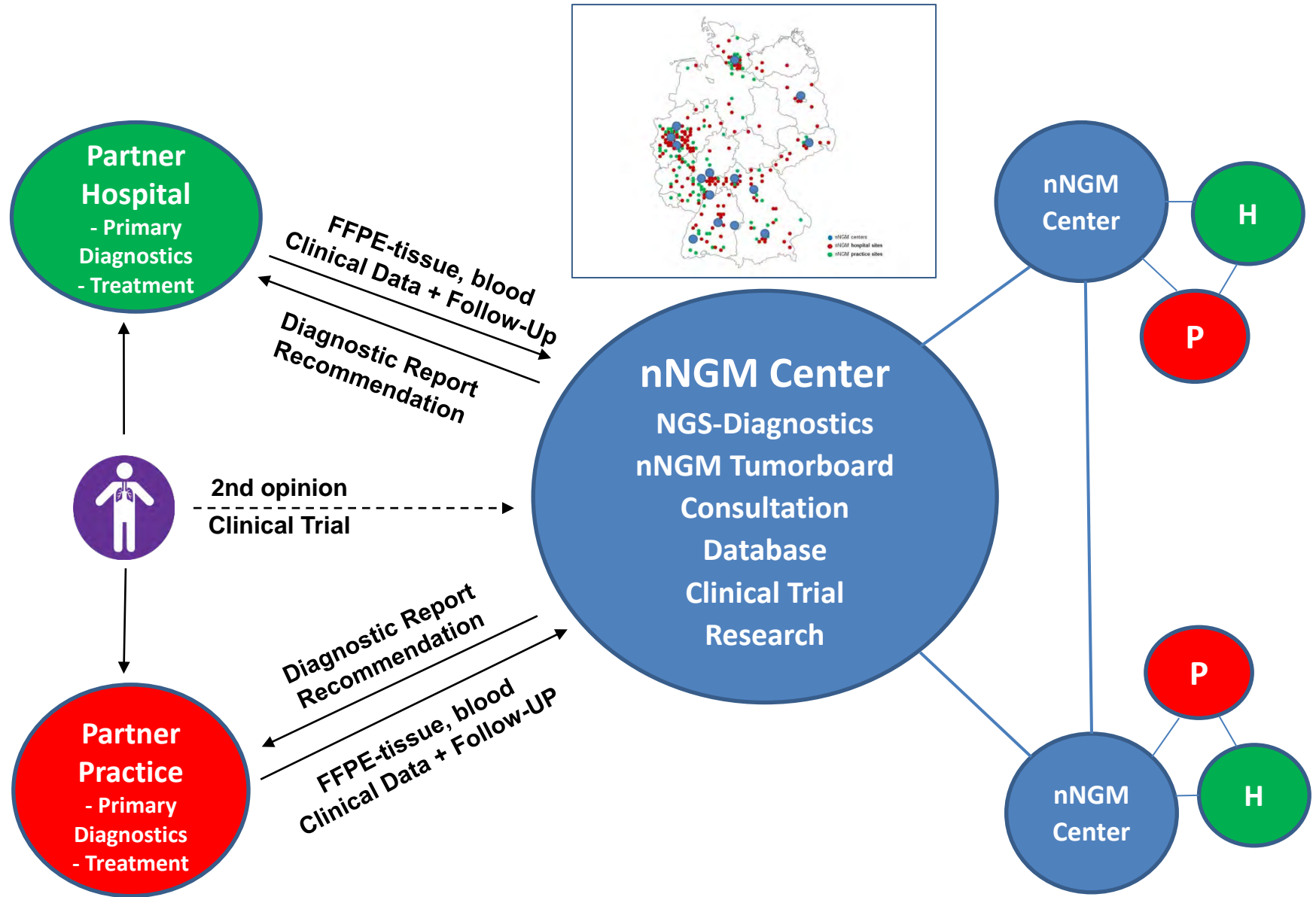
- nNGM centers
- nNGM hospital sites
- nNGM practice sites

**2018: molecular diagnostics
of ca. 10.000 pts.
with advanced NSCLC**

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

> Personalized cancer medicine becomes reality

Our vision for all patients with (lung) cancer



Thank you !



nNGM

National Network
Genomic Medicine
Lung Cancer

- nNGM-centers
- Task Force - speakers
- Center manager
- nNGM-office

- **all regional network partners**

LungCancerGroup
Cologne

 **DKTK**
Deutsches Konsortium für
Translationale Krebsforschung

- **all patients and their families**

THE ROSI DERS
BRIDGING ROSI+ PATIENTS TO RESEARCH

- **Deutsche Krebshilfe**
- **Ministerium für Kultur und Wiss. NRW**
- **BMBF**



Ministerium für
Kultur und Wissenschaft
des Landes Nordrhein-Westfalen



Bundesministerium
für Bildung
und Forschung



... and further health insurances