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

Speaker: J.Wolf, R.Büttner
Scientific coordination: A Kron
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Hospitals and private practice-based oncologists

Patient advocacy groups

Allocation to clinical trials

genotype + recommendation

tumor tissue

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

Health Insurance Companies

Cancer Registry CIO
Cancer Registry NRW

Translational Genomic Research

Network Genomic Medicine
Lung Cancer

Speaker: J. Wolf, R. Büttner
Scientific coordination: A. Kron
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**University Hospital Cologne**
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**Translational Genomic Research**
**Health Insurance Companies**
**Cancer Registry CIO**
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**Network Genomic Medicine: Lung Cancer**
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Translational Genomic Research
Health Insurance Companies
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Speaker: J.Wolf, R.Bütter
Scientific coordination: A Kron
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

- Substitution
- Deletion
- Insertion
- Inversion

Complex structural alterations

Chromosomal copy-number alterations

- Normal (cn=2)
- Amplification
- Deletion
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 genomic evolution of lung adenocarcinoma

Pao et al., Lancet Oncol 2011
Development of sequencing output and costs
Genomic information: a new disruptive standard of personalized oncology

EGFR inhibitor, no selection

Survival chemo
Survival EGFRi, no selection
Survival EGFRi, selection

HR = 0.72, p = 0.001
Erlotinib (Median) = 6.7 Monate (n=488)
Placebo (Median) = 4.7 Monate (n=243)
1-Jahres-Überlebensrate = 31%
1-Jahres-Überlebensrate = 21%

EGFR inhibitor, selection

HR 0.169 (Cl₉₅ 0.07-0.41)
mOS 31.5 vs 9.6, P < 0.001

Shepherd et al., NEJM 2005
Seidel et al., Science Transl Med 2013
The role of genomics in clinical oncology

• First single breakthrough technology to change cancer patients’ lifes
• New opportunities for discovery and...
• ...diagnostics alike
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.

**NSCLC stage IIIB, IV**

**Non-squamous cell carcinoma**
- **EGFR** ca. 12%
- **ALK** ca. 4%
- **ROS1** ca. 2%
- **BRAF V600** ca. 1.5%

- Erlotinib
- Gefitinib
- Afatinib
- Crizotinib
- **Resistance mutations**
  - T790M
  - Osimertinib
  - Lorlatinib
  - Brigatinib

**Squamous cell carcinoma**
- **PD-L1 (tumor cells)**

- **PDL1 > 50%**
  - Pembrolizumab
- **PDL1 – / < 50%**
  - Pembrolizumab + Chemotherapy

**Targeted therapy**

**Chemotherapy**

- Nivolumab: PD-L1 independent
- Pembrolizumab: only PD-L1 +
- Atezolizumab: PD-L1 independent
Systemic therapy of NSCLC is increasingly guided by biomarkers

NSCLC stage IIIB, IV

Non-squamous cell carcinoma  Squamous cell carcinoma

**EGFR** ca. 12 %  **ALK** ca. 4 %  **ROS1** ca. 2 %  **BRAF** V600 ca. 1.5 %

- Erlotinib
- Gefitinib
- Afatinib
- Crizotinib
- Dabrafenib + Trametinib

**PD-L1 (tumor cells)**

- PDL1 > 50%  Pembrolizumab
- PDL1 – / < 50%  Pembrolizumab + Chemotherapy

**Resistance mutations**

- T790M
- **Osimertinib**
- **Lorlatinib**
- **Brigatinib**

**Chemotherapy**

**Nivolumab**: PD-L1 independent

**Pembrolizumab**: only PD-L1 +

**Atezolizumab**: PD-L1 independent

**Nivolumab: PD-L1 independent**

**Cologne**: **NGM** diagnostic panel

18 Genomic Alterations
5 different Immunotherapies >> Cologne
Immuno/Chemotherapies >> NGM diagnostic panel
Network Genomic Medicine: Integrating High-end Molecular Diagnostics and Oncological Expertises
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 3rd gen. EGFR inhibitors

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

Jänne et al., NEJM 2015
3rd gen. EGFR-TKI as 1st line therapy are superior to 1st gen. inhibitors

Initial biopsy

Erlotinib, Gefitinib (8-10m)

T790M

Osimertinib (8-10m)

PD: rebiopsy

EGFR del 19 L858R

Osimertinib (18.9m)

Initial biopsy

Erlotinib, Gefitinib (8-10m)

T790M

Osimertinib (8-10m)

Osimertinib (18.9m)

PFS

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

FLAURA
Phase III
Osimertinib vs. Standard EGFR-TKI

Soria et al, NEJM 2018
Overcoming resistance by structure-based compound design

Zhou et al., Nature 2009
Osimertinib first-line suppresses emerging T790M

G724S and C797S are the most frequent resistant mutations after osimertinib.

EGFR\textsuperscript{G724S} osimertinib resistance mutation sensitive to 2\textsuperscript{nd} gen. EGFR inhibitor afatinib

Fassunke et al, Nature Comm. Nov. 2018
Jana Fassunke,...D. Rauh, M. Sos, Nat Comm, Nov 2018
Sequential therapy in EGFRmut NSCLC: increasingly molecularly guided

1st gen. EGFR-TKI PFS: 10 m
T790M+ Osimertinib PFS: 10 m
T790M- Chemo PFS: 5 m

2nd gen. EGFR-TKI PFS: 14.7 m (dacom.)
T790M+ Osimertinib PFS: 10 m
T790M- Chemo PFS: 5 m

alternatively: 1st gen. EGFR TKI + bevacizumab:
T790M+: PFS 16m / T790M-: PFS 10m
Osimertinib PFS: 19 m

EATON Trial
3rd.gen EGFR-TKI + MEKinh.
Prevent Resistance

PD: rebiopsy

Erlo/Gefitinib
Osimertinib
Chemo-therapy

EGFR C797S
Afatinib
Osimertinib
EGFR G724S
HER2 amp.
Crizotinib
Osimertinib
MET amp.
KRAS Mut
Chemo-therapy

EATON Trial
3rd.gen EGFR-TKI + MEKinh.
Prevent Resistance
Genomic profiling identifies outcome-relevant mechanisms of innate and acquired resistance to third-generation EGFR TKI therapy in lung cancer

Michels, Heydt et al, JCO Prec. Oncology in press
EGFRmut. NGM cohort: overall survival dependent on therapy

1: chemo only; 2: 1 gen. TKI; 3: more than 1 TKI

<table>
<thead>
<tr>
<th></th>
<th>Gesamtzahl</th>
<th>Anzahl der Ereignisse</th>
<th>Median in Monaten</th>
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<tr>
<td>1</td>
<td>129</td>
<td>57</td>
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<tr>
<td>2</td>
<td>335</td>
<td>103</td>
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<tr>
<td>3</td>
<td>31</td>
<td>8</td>
<td>56,000</td>
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<tr>
<td>Gesamt</td>
<td>495</td>
<td>168</td>
<td>35,000</td>
</tr>
</tbody>
</table>

P < 0,0001

3: 1st gen. EGFR-TKI followed by 3rd gen. EGFR-TKI

Kron et al, ASCO 2017
EGFRmut. NGM cohort: overall survival dependent on therapy

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
Application of Artificial Intelligence (AI) Predicting Efficacy of Immune Therapies
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
2nd evaluation of the Network Genomic Medicine (NGM, 2016)

Non-squamous NSCLC (n=4244)

- KRAS 35%
- EGFR 13%
- WT 37%
- Others (RET, FGFR) 1%
- PIK3CA 1%
- DDR2 1%
- HER2 1%
- ROS1 1%
- ALK 2%
- MET 4%

Squamous NSCLC (n=1489)

- KRAS 19%
- WT 68%
- FGFR1 19%
- PIK3CA 4%
- Others 1%
- BRAF 1%
- EGFR 1%
- DDR2 2%
- MET 2%
- KRAS 2%

Publications of NGM subcohorts
Genetically-determined NSCLC subgroups
2nd 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
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)

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

Translational program
- Pathology - AG Thomas - AG Sos - AG Ulrich - AG Pfeifer - AG vBergwelt
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?
Hypothesis
Crizotinib is effective and safe in ROS1-positive lung cancer (N=30 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)

Management team
LCGC, CTCC, SLCG
Crizotinib in ROS1-positive NSCLC
EUCROSS trial: Overview and challenges

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

Management team
LCGC, CTCC, SLCG

Financial support
Pfizer

Drug supply
Pfizer
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Sites
LCGC, SLCG, collaborating centers
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Sites
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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

**Local assessment** vs **BIRC**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Local assessment</th>
<th>BIRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR (%)</td>
<td>70.0 (n=21; 95% CI, 50.6-85.3)</td>
<td>72.4 (n=21; 95% CI, 52.3-87.3)</td>
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<tr>
<td>Median PFS (months)</td>
<td>20.0 (95% CI, 10.09-n.r.)</td>
<td>20.0 (95% CI, 9.6-NR)</td>
</tr>
<tr>
<td>PFS at 24 months (%)</td>
<td>45.6 (95% CI, 25.6-65.6)</td>
<td>45.8 (95% CI, 25.8-65.8)</td>
</tr>
</tbody>
</table>

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

Sebastian Michels – ICPeRMed 2018
Advantage of early trial participation
Patients received crizotinib treatment in clinical trials years before approval

- **04/2006**
  - Phase I, USA (PROFILE 1001)

- **01/2010**
  - Phase II, Cologne (PROFILE 1007)

- **10/2012**
  - EMA approval (2.-Linie)

  **Crizotinib in ALK-positive adNSCLC**

- **05/2014**
  - Phase II, Cologne (EUCROSS, IIT)

- **08/2016**
  - EMA approval (1.-Linie)

  **Crizotinib in ROS1-positive adNSCLC**

  - Advantage
    - 2 years 9 months
  - Advantage
    - 2 years 3 months
## 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**

**Cooperating platforms**
- Spanish Lung Cancer Group
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- Pathology
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- AG vBergwelt

**LCGC IITs and projects**
- ERLOPET
- TransMET
- TRY
- EUCROSS
- BIOLUMA
- EATON
- FIND

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
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

Partner sites: hospitals & private practices in NRW

Genotyping + consultation

FFPE tissue + data

Local pathology

University Hospital of Cologne
Institute of Pathology and Department I of Internal Medicine
(Lung Cancer Group Cologne)

Multiplex Molecular Diagnostics
Next Generation Sequencing

Clinical trials

Evaluation of:
- therapy
- outcome
- costs

cancer register CIO

cancer register 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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194 partner sites nationwide (101 hospitals & 93 private practices)

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Ca. 5,000 diagnostics p.a. = 10% of lung cancer incidence in Germany

Clinical trials

Evaluation of:
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1st NGM Evaluation 2013:
OS benefit with personalized therapies

The Clinical Lung Cancer Genome Project and Network Genomic Medicine, Sci Transl Med 2013
NGS-based genotyping + consultation potentially covered by ICC for ca. 53% of all annually newly diagnosed inoperable lung cancer patients in Germany
Data architecture

- Partner sites
- External pathology (primary diagnostics)
- NGM office
- NGM pathology (multiplex diagnostics)
- Research associations
- Health insurance companies
- Lung cancer patients
2nd NGM Evaluation 2018:
OS benefit with sequential therapies

Michels et al., JCO Precision Oncology 2018
Kron et al., Ann Oncol. 2018
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
Studienübersicht

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<th>Marke/Bezeichnung</th>
<th>Titel</th>
<th>Indikation</th>
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<tr>
<td>CEGF816X2102</td>
<td>Eine multizentrische, offene Phase-II-Dosisfindungsstudie mit EGFR</td>
<td>Die Studie ist multizentrisch und offen. EGFR ist der Marker.</td>
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<td>Study zur Charakterisierung der Wirksamkeit von Cisplatin und</td>
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<td>In Patienten mit fortgeschrittenen</td>
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<td>Inhibitoren der 1. und 2. Generation</td>
<td>EGFR ist der Marker für die Wirksamkeit von Q&amp;A und Blockade.</td>
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Studienübersicht CEGF816X2102

Status: Aktive Studie | Marker: EGFR

- **Titel**
  Eine multizentrische, offene Phase-II-Dosisfindungsstudie mit EGFR-Blockade in Kombination mit Cisplatin und Quantum-Amply-Konzepten in Patienten mit fortgeschrittenen NSCLC; Resistent auf EGFR-Inhibitoren der 1. und 2. Generation.

- **Zentrale Studiennummer**

- **Indikation**

- **Studienziel & Fragestellung**

- **Patientenmerkmale**

- **Studienplan**

- **Zuständigkeiten der Gesamtstudie**
SAVE THE DATE: 2nd Cologne Conference on Lung Cancer

2nd Cologne Conference on Lung Cancer
26 – 27 JUNE 2019 | GERMANY

www.cologne-clc.com
The Referring Doctor’s Strategy

Achim Rothe, Cologne – Med. Oncologist in Private Practice
Regional lung cancer network

Oncologist in Private Practice
Local Pathology
Peripheral Hospital

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

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

Comprehensive Genotyping
Consultation
Coordination

Translational Genomic Research

Cancer Registry CIO
Cancer Registry NRW
Local implementation

- Patient with suspected lung cancer
  - General practitioner
  - Oncologist in private practice > initiation of diagnostics
    - Lung cancer center > diagnostics and evaluation of therapy
      - Clinical study
  - Standard personalised therapy
    - Off-label personalised therapy
What a patient expects from a local oncologist...

- Direct communication and comprehensive information
- Accessability
- 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 accessability 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
The Patient’s Perspective
Bärbel Söhlke, Düsseldorf – Patient
The payer’s perspective
Motivation of health insurance company to support nNGM

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 outpatient 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:

<table>
<thead>
<tr>
<th>Patients</th>
<th>Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGF-R (Gefitinib, Erlotinib, Afatinib, Osimertinib)</td>
<td>344 (3.8%)</td>
</tr>
<tr>
<td>ALK, ROS (Crizotinib, Ceritinib)</td>
<td>107 (1.2%)</td>
</tr>
<tr>
<td>Pembrolizumab (PD1)</td>
<td>895 (9.6%)</td>
</tr>
<tr>
<td>Nivolumab (PD1)*</td>
<td>748 (8.3%)</td>
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* 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: the time lag between evidence and patient benefit

- 22,000 incident advanced NSCLC in 2017 (AOK)
- 9,000 with systemic therapy

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<tr>
<td>EGF-R (Gefitinib, Erlotinib, Afatinib, Osimertinib)</td>
<td>344 (3.8%)</td>
<td>5.5% - 10%</td>
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<td>895 (9.6%)</td>
<td>20-25% in 2017**</td>
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<td>Nivolumab (PD1)*</td>
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<td>Off-label use</td>
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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

<table>
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<th>Lung- Cancer Centers n=2757</th>
<th>Other hospitals n=4917</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGF-R (Gefitinib, Erlotinib, Afatinib, Osimertinib)</td>
<td>113 (4.1%)</td>
<td>204 (4.2%)</td>
</tr>
<tr>
<td>ALK, ROS (Crizotinib, Ceritinib)</td>
<td>29 (1.4%)</td>
<td>63 (1.3%)</td>
</tr>
<tr>
<td>Pembrolizumab (PD1)</td>
<td>331 (12%)</td>
<td>517 (10.5%)</td>
</tr>
<tr>
<td>Nivolumab (PD1)*</td>
<td>316 (11.5%)</td>
<td>567 (11.6%)</td>
</tr>
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* off-label use

- 9,000 patients with incident advanced NSCLC and systemic therapy
- 80% inpatient care
- 20% only ambulatory care
- 37% certified lung cancer center
- 63% other hospitals

80% inpatient care

20% only ambulatory care

37% certified lung cancer center

63% other hospitals

* 80% inpatient care
* 20% only ambulatory care
* 37% certified lung cancer center
* 63% other hospitals
* 9,000 patients with incident advanced NSCLC and systemic therapy
* EGF-R (Gefitinib, Erlotinib, Afatinib, Osimertinib)
* ALK, ROS (Crizotinib, Ceritinib)
* Pembrolizumab (PD1)
* Nivolumab (PD1)*

* 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
Next Steps

Jürgen Wolf, Cologne – Medical Oncologist
Network Genomic Medicine:
Founded in 2010 with funding from Ministry for Innovation and Research NRW

Hospitals and private practice-based oncologists

Patient advocacy groups

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

Health Insurance Companies

Genotype + recommendation
tumor tissue

Allocation to clinical trials

Translational Genomic Research

Cancer Registry CIO

Cancer Registry NRW

Network Genomic Medicine Lung Cancer

Speaker: J.Wolf, R.Büttner
Scientific coordination: A Kron
Network Genomic Medicine:
Founded in 2010 with funding from Ministry for Innovation and Research NRW

NGM = proof of principle for broad implementation of molecular diagnostics and personalized lung cancer care

Evaluation of personalized therapy:
- molecular epidemiology
- outcome
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NGM = proof of principle for broad implementation of molecular diagnostics and personalized lung cancer care

Next step: to enroll the model nationwide

NGM > nNGM
country Network Genomic Medicine

Allocation to clinical trials

Translational Genomic Research

Health Insurance Companies

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

Cancer Registry CIO

CGC Cancer Registry NRW

Network Genomic Medicine: Founded in 2010 with funding from Ministry for Innovation and Research NRW

Speaker: J. Wolf, R. Büttner
Scientific coordination: A Kron
national Network Genomic Medicine
Lung Cancer
Funding by the German Cancer Aid since 04/18

15 German Oncology Centers of Excellence

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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)
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J Wolf (Köln)
R Büttner (Köln)
C v Kalle (Heidelberg)
Development of regional networks

Current status: regional partners

2018:
ca. 10,000 patients with advanced lung cancer and molecular diagnostics
> ca. 1/3 of the target population
Thank you!

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

- all the regional network partners of nNGM and NGM

- all the patients and their families

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

- Health Insurance Companies

... and many others health insurances