Meeting protocols

- To protect the quality of the audio for everybody please stay on “Mute” throughout the meeting.

- We encourage all participants to join the interactive discussion in the Chat box: ask questions, share thoughts and comments.

- Please note that the meeting will be recorded.

#LungCancerRoundtable  europeancancer.org
Community 365 Roundtable
Meeting on Lung Cancer

Agenda:

15:05-15:20  Essential Requirements for Quality Cancer Care: Lung Cancer
Yolande Lievens, Co-Chair of the Quality Cancer Network

15:20-15:30  Open Discussion

15:30-15:50  Early Detection and Screening
Co-Chair: Françoise Bartoli, VP, Head of Europe and Canada, Oncology Business, AstraZeneca
Presentation: Giorgio Scagliotti, Professor of Oncology, University of Turin and Chief of the Medical Oncology Division at the S. Luigi Hospital

15:50-16:00  Open Discussion
Community 365 Roundtable Meeting on Lung Cancer

16:00-16:20  Molecular Diagnostics in Lung Cancer – Considerations and Relevance for Treatment Selection

Co-Chair: Geoff Oxnard, Vice President, Global Medical Lead, Liquid Franchise at Foundation Medicine

Presentation: Matthew Krebs, Clinical Senior Lecturer in Experimental Cancer Medicine, University of Manchester and Consultant in Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK

16:20-16:30  Open Discussion

16:30-16:50  The Dutch Lung Cancer Audit: Nationwide Quality of Care Evaluation Using Quality Indicators

Co-Chair: Ouzna Morsli, EMEAC Oncology Medical Lead at MSD

Presentation: Hans J.M. Smit, MD, PhD, Pulmonologist Rijnstate Hospital, Chairman of the Dutch Lung Cancer Audit, Arnhem, The Netherlands and Rawa Ismail, PharmD and PhD Candidate DICA

16:50-17:00  Open Discussion
Our Quality Cancer Care Network

- Prevention Network
- Quality Cancer Care Network
- Survivorship and Quality of Life Network
- Inequalities Network
- Workforce Network
- HPV Action Network
- Health Systems and Treatment Optimisation Network
- Digital Health Network

Special Network: Impact of COVID-19 on Cancer
Our Quality Cancer Care Network
European Cancer Organisation Essential Requirements for Quality Cancer Care (ERQCC): Lung cancer

Thierry Berghmans, Yolande Lievens, Matti Aapro, Anne-Marie Baird, Marc Beishon, Fiorella Calabrese, Csaba Dégi, Roberto C. Delgado Bolton, Mina Gaga, József Lövey, Andrea Luciani, Philippe Pereira, Helmut Prosch, Marika Saar, Michael Shackcloth, Geertje Tabak-Houwaard, Alberto Costa, Philip Poortmans
Community 365 Roundtable on Lung Cancer

Legacy from this meeting will include:

• Action report to be published in early January
• From tomorrow, video and slides on our website europeancancer.org/resources
• Follow up with EU Commission ahead of publication Europe's Beating Cancer Plan
• Next steps on implementation of Essential Requirements in our Quality Cancer Care Network
Essential Requirements for Quality Cancer Care: Lung Cancer

Yolande Lievens
Co-Chair of the Essential Requirements for Quality Cancer Care: Lung Cancer
Lung cancer: So much more to do

• In 2018, the estimated incidence of lung cancer in EU countries was around 365,000 with mortality nearly 300,000.

• Lung cancer sadly remains a poor prognosis tumour with 5-year survival rates at a very low level. Men represent about two-thirds of mortality – nearly 200,000 were projected to die from lung cancer in 2018.

• Opportunities for improvement in prevention, care and treatment remain insufficiently exploited.

• Better organisation of care, and ensuring patient access to key members of the multidisciplinary and multi-professional healthcare team, can drive up both quality of care and outcomes.

• The Essential Requirements for Quality Cancer Care: Lung Cancer aims to help countries bridge that gap
The Lung Cancer manuscript has been produced by the European Cancer Organisation as part of the Essential Requirements for Quality Cancer Care (ERQCC) programme.

The European Cancer Organisation Essential Requirements for Quality Cancer Care (ERQCC) are written by experts representing all disciplines involved in cancer care in Europe.

They give patients, health professionals, managers and policymakers a guide to essential care throughout the patient journey.
Some section highlights

- A diagnosis and treatment summary
- Treatment centre recommendations
- Recommendations on care pathways and timelines
- Description and outline of the multidisciplinary team
- Recommendations on research and education

Patient involvement, access to information and transparency

Performance and quality recommendations
Understanding the particularities

The challenges section of the ERQCC paper helps audiences understand
- what makes lung cancer particular
- how organisational and health service response must adapt to this

such as

- The high rate of diagnosis of lung cancer at advanced stages is a major challenge for improving outcomes, and makes the option of lung cancer screening interesting.
- Improved strategies at primary care level are highlighted, such as lowering barriers to access - and to demanding - imaging, and equipping GPs with risk prediction tools.
- Diagnosing and staging lung cancer is complex. It is essential that experienced specialists (e.g. radiologists, pulmonologists, pathologists, nuclear medicine specialists) determine results from imaging and pathological samples. A successful management plan, especially for radical interventions, depends on their input to the MDT.
The challenges section of the ERQCC paper helps audiences understand:
- what makes lung cancer particular
- how organisational and health service response must adapt to this

such as:

- **Optimal treatment of lung cancer is particularly challenging**, as patients may be older and have important comorbidities, requiring strong multidisciplinary knowledge, commitment and interaction to tailor the treatment to each individual patient.

- **Patients with lung cancer are a neglected population for psychosocial needs** compared with some other cancers, partly owing to the stigma of the disease as being self-inflicted through smoking, and they report increased distress as a result.
Pathway & Organisation: Getting it right!

**The ERQCC: lung cancer**
- provides advice on improving pathway management for lung cancer patients
- highlights good practice on cancer centre organisation

- After a diagnosis, the patient must know which professional is responsible for each step in the treatment pathway and who is following the patient during the journey (usually called a case manager or patient navigator)
- Follow-up, support and care for long-term survivorship, as well as palliative care, must be part of a care pathway.
- There is direction towards care and treatment for lung cancer performed in higher volume centres. European countries taking notable steps in this direction:
  - **Denmark** - now carries out surgery in just 4 centres, and also has fewer locations where lung cancer is diagnosed and evaluated, reduced to 13 sites from about 50 previously
  - **Germany** - the target for a certified lung cancer centre is 200 cases a year (all new presentations)
Defining the core and extended MDT

Treatment strategies for all patients with lung cancer must be decided on, planned and delivered as a result of consensus among a core MDT that comprises the most appropriate members for the particular diagnosis and stage of cancer, and patient characteristics and preferences, with input from an extended group of professionals.
Requirements for professions: Examples

Essential requirements: radiation oncology

- Radiation oncology departments treating lung cancer must have access to up-to-date radiotherapy technology and techniques such as IMRT and SBRT, ideally on-site or at a centre through a formal collaborative agreement that includes a common MDT.
- Radiation oncologists must know the indications of radiotherapy for lung cancer, and the place, expected efficacy and potential side-effects of thoracic radiotherapy in multidisciplinary treatment regimens. They must have a special interest and expertise in the multidisciplinary treatment of lung cancer and of other thoracic malignancies to select the optimal treatment for each patient, considering the specific oncologic situation and comorbidities.
- Multimodal imaging including a CT in treatment position and/or a PET/CT scan are mandatory to define the target volume, along with pathological information obtained through mediastinal staging – either EUS-EBUS or mediastinoscopy – in the case of locally advanced disease.
- Radiation oncologists treating lung cancer must have a team of radiation therapists, dosimetrists and medical physicists with expertise in lung cancer and thoracic malignancies.
- Radiation oncologists must be aware of ongoing clinical trials and their methodology performed at their centre or in associated centres.
- The radiation oncology centre must have regularly updated protocols for radiotherapy and concurrent chemoradiotherapy for lung cancer based on international guidelines.
- Image guidance, motion management and adaptive radiotherapy policies and quality assurance guidelines must be clearly described and documented. External quality assurance audits are highly recommended.
- Radiation oncologists must follow up patients to act on early or late toxicity, and in case of relapse.
Requirements for professions: Examples

**Essential requirements: nursing**

- Nurses must conduct holistic assessments to predict inpatient and out-patient care needs to ensure personalization of care.
- Nurses must conduct collaborative reviews of the efficacy throughout the patient journey of shared care.
- Nurses must conduct holistic assessments and determine the most suitable and family-oriented care trajectories.
- Nurses must conduct holistic assessments and determine the most suitable care trajectories at the point of entry.
- Nurses must conduct holistic assessments to determine the most suitable care trajectories.
- Cognitive impairment and advanced age must be used in the assessment.

**Essential requirements: palliative care**

- The MDT must offer optimal supportive and palliative care at the earliest opportunity.
- There must be access to a dedicated palliative care unit with a specialist team that provides expert outpatient and inpatient care and good knowledge of cancer disease and cancer treatments.
- The palliative care team must include palliative care physicians and specialist nurses, working with an extended team of social workers, psychotherapists, physiotherapists, occupational therapists, dieticians, pain specialists and psycho-oncologists.
- The palliative care team must have experience of taking care of frail older patients and their families.
- To ensure the continuity of care at home, the palliative care team must work with community/primary care providers.
- Palliative care specialists and oncologists must aspire to meet the standards of ESMO Designated Centres of Integrated Oncology and Palliative Care (http://www.esmo.org/Patients/Designated-Centres-of-Integrated-Oncology-and-Palliative-Care).

**Essential requirements: interventional radiology**

Interventional procedures must be performed by an experienced interventional radiologist, with access to appropriate interventional CT imaging and 3D-CT imaging are recommended. Interventional radiologists must be available to the MDT to discuss the use of local ablative techniques for treating patients who are not amenable to, or combined with, surgery.

**psycho-oncology/psychosocial care**

- Provided at all stages of the disease and its impact on patients and their partners and families.
- Psychological assessment by the healthcare team.
- Administered tool (such as a distress thermometer) used to determine level of distress; above that level there must be further screening for anxiety and depression, and appropriate professional, such as a mental health professional, is involved.
A lung cancer centre must develop:

- **Performance measurement metrics/quality indicators** based on the essential requirements in this paper and on clinical guidelines, in alignment with national requirements and legislation
- **Operational policies** to ensure the full benefits of a coordinated clinical pathway based on published guidelines
- **Accountability** within the governance processes in individual institutions
- **Systems** to ensure safe and high-quality patient care and experience throughout the clinical pathway
- **Effective data management** and **reporting systems**
- **Engagement with patients, their carers and support groups** to ensure reporting of patient outcomes and experience.
Some final words on improving lung care

Lung cancer
• includes variable disease entities and patient groups;
• requires a large range of knowledge and expertise over the entire care pathway;
• from professionals that work in a well-structured and organised manner.

Educational and awareness programs should support that available research evidence is accessible, translating into optimal outcome.

Initiatives such as ERQCC: lung cancer should not remain a static endeavour but should continuously integrate optimised treatment and health system approaches and be informed by data collected in clinical trials as in real-life practice.
Thank you to the paper contributors!
Open Discussion

Please use the Chat feature to ask questions and make comments
Redefining the future for lung cancer patients in Europe

Co-Chair:
François Bartoli, VP, Head of Europe and Canada, Oncology Business, AstraZeneca
Accelerating advances for lung cancer patients through collaboration

Giorgio Scagliotti, Professor of Oncology, University of Turin and Chief of the Medical Oncology Division, S. Luigi Hospital
Eight pillars of the current IASLC strategic plan

- Education
- Research
- Membership
- Int’l Development
- Governance
- Policy
- Funding
- Strategic Partnerships
Globally lung cancer is the leading cause of cancer death with 1.8 million lives lost annually

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<th>% at diagnosis</th>
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<td>68–92%</td>
<td>26%</td>
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<td>Stage II</td>
<td>53–60%</td>
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<tr>
<td>Stage IV</td>
<td>0–10%</td>
<td>40%</td>
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</tbody>
</table>

Globally lung cancer is the leading cause of cancer death with 1.8 million lives lost annually.

Staging: Improving Lung Cancer Staging through International Collaboration

• For more than 20 years, the IASLC has provided valuable recommendations for the TNM classification of lung cancer

• IASLC is currently gathering data to inform the 9th edition of the TNM Staging System, which for the first time, will include new data elements such as gene mutations, fusions, and copy number alterations and protein expression level.

• The goal of these additional tumor characteristics is to significantly enhance the accuracy of the Staging System, leading to more precise treatment regimens and increased patient survival.

• As of November 2020, the following number of cases have been collected from over 20 countries: Lung Cancer: 54,789, Mesothelioma: 436, Thymic malignancies: 7,183
We are at a critical moment in the fight against lung cancer

In 2018 alone, 1.8 million people died from lung cancer\(^1\)

Every 18 seconds, a life is lost to lung cancer\(^1\)

40% are diagnosed after the disease has spread beyond the lung, worsening prognosis\(^2\)

Only 1 in 5 patients are alive 5 years after diagnosis\(^3\)

The Time For Change Is Now

Diverse perspectives enable our four founding partners to identify needs more precisely, while our depth of resources help us to amplify impact as we work to **eliminate lung cancer as a cause of death**

Project partners: Merck - BMS - Genentech - Lilly - Novartis
# Lung Ambition - The Mission

## Vision
What does the coalition aim to achieve?

As global partners with a common and enduring commitment, the coalition aims to one day **eliminate lung cancer as a cause of death**.

## Mission
Why should the coalition exist?

As a coalition, we can **accelerate progress** by amplifying the multi-disciplinary expertise of our partners.

## Goals
What do we want to do?

Together, we can shape the environment to improve outcomes for patients with lung cancer. As a first goal we will use the evidence, advance the science and motivate the community to **double 5-year survival in lung cancer by 2025**.

## Strategic Focus
How will we achieve it?

We will deliver on the mission through 3 key areas of focus:

- A commitment to **early screening & diagnosis**
- A promise to deliver **precision, curative treatments**
- A passion for ensuring **quality care** for patients
Focusing on Today and Future Potential

Screen & Diagnose Early

1. Screening Access & Policy
2. Screening Rates
3. New Technology (ctDNA)

Deliver Innovative Medicine

1. Early-Stage Disease
2. Resistance Mechanisms
3. Clinical Endpoints

Enhance the Quality of Care

1. Long-term Survivorship
2. Access
3. Standards of Optimal Care

Screen & Diagnose Early

Deliver Innovative Medicine

Enhance the Quality of Care

Focusing on Today and Future Potential
LDCT screening trials results: lung cancer mortality can be reduced

- large size trial ( > 50,000)
  - diameter > 3 mm  no risk modulation
  - 3 rounds / 2 years

- medium size trial ( > 15,000)
  - volume > 50 mm³ + VDT  no risk modulation
  - 4 rounds / 6.5 years

- small size trial ( > 4,000)
  - volume > 60 mm³ + VDT + PET  LDCT risk modulation
  - 5+ rounds / 8-10 years


deKoning H, WCLC 2018; Toronto


NLST
NELSON
MILD
Screening of Lung Cancer: key issues

- Evidence from RCTs
- LDCT technology and risk
- Overtreatment & surveillance
- Benefits beyond LC detection
- Liquid biopsy & biomarkers
- Boosting prevention with LDCT
- Personalized strategy
- Implementation challenges
- Screening in the covid-19 time
Benefits and Harms of Lung Cancer Screening by Low-Dose Computed Tomography: a systematic review and meta-analysis

Passiglia F. et al. unpublished data, paper submitted to a peer reviewed journal
SPIRAL
Screening planning and implementation
Early Lung Imaging Confederation (ELIC)

Lung cancer imaging database and computational analysis environment designed to enable the study of extremely large collections of quality-controlled internationally assembled CT chest images and associated biomedical data.

ELIC Hub and Spoke Model
ELIC Moving Forward

✓ 'Overall uptake of low-dose CT-screening needs to increase, if we are going to make a further dent in the lung-cancer mortality'
  • Awareness Campaigns
  • Educational Efforts
  • Videos/Webinars
  • Podcasts with Multidisciplinary Participation
  • Workshops

✓ Stratification of the indeterminate nodule on the screening scans

✓ Detection of squamous-cell and small-cell lung cancer earlier will be of importance

✓ Application of Artificial Intelligence, Machine and Deep learning will pick up relevant images for further invasive procedures and non-invasive bio-marker studies
  • Precise volumetric segmentation of lung nodules automatically -- both detected and user found (Deep Learning will reduce variability)
  • Benign vs. Malignant
Biomarkers in lung cancer screening: achievements, promises and challenges

Major Pathologic Response Project

Step 1
MPR multidisciplinary recommendations paper for standardized tissue processing and pathologic assessment

Step 2
Conduct interobserver reproducibility study based on recommendations for assessment

Step 3
Collect data to compare pathologic response and other biomarkers to survival – ultimate goal is surrogate marker for outcome
ILC2 invites local PAGs around the world to develop and submit projects with a potential to transform care and improve survival of lung cancer pts.

60 applications received
30 applications were reviewed
14 were selected by the committee for a total of $1,035,812 to be distributed during this application cycle

### Awardees by Region

- **United States**: $100,000
- **United Kingdom**: $98,918
- **KENYA**: $95,335
- **Egypt**: $93,728
- **Australia**: $90,831
- **Canada**: $89,000
- **United States**: $25,000
- **Rwanda**: $25,000
- **Costa Rica**: $25,000
- **Argentina**: $24,000

**Grand Total**: $1,035,812

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**Round 2 is Now Open!**

To complete your application please click here [link]

ILC2 grant applications are reviewed and selected by the four founding partners of the Lung Ambition Alliance: the Global Lung Cancer Coalition, Guardant Health, the International Association for the Study of Lung Cancer and AstraZeneca. Funding for the IL2 grant is provided by AstraZeneca.

All applications must be completed by 31 December 2020.
LAA: Other Funded Projects

**COVID-19 Research Grants**
Junior Faculty Research Grants for the Study of Lung Cancer and COVID-19
3 Grants for $50,000 each
Goal: Obtain preliminary data to enable successful competition for national peer-reviewed grants

With this effort Novartis and Eli Lilly became Project Partners of LAA

- **TERAVOLT Project**
- The IASLC, through the LAA, funded TERAVOLT.
- Goal: Understanding the impact of COVID-19 on thoracic malignancies,
  - Risk factors associated with morbidity and mortality
  - Therapies that may impact survival
  - Guidance on the management of patients
Developing Partnerships through Data Sharing with Academic Institutions, Societies & Industry

- Enhance and improve DATA SHARING
- Recognizing Patterns in Large Volume of Data
- Identifying Characteristics that cannot be perceived by the human brain, e.g., mutations with non-invasive techniques
- Ultimately improve the survival of lung cancer patients
The LungAmbition Alliance

Accelerating advances for people with lung cancer.
Thank you!
Open Discussion

Please use the Chat feature to ask questions and make comments
Final Remarks

Co-Chair: 
Françoise Bartoli, VP, Head of Europe and Canada, Oncology Business, AstraZeneca
Molecular Diagnostics in Lung Cancer – Considerations and Relevance for Treatment Selection

Co-Chair:
Geoff Oxnard, Vice President, Global Medical Lead, Liquid Franchise at Foundation Medicine
Precision cancer care & precision cancer diagnostics

EMPIRIC CANCER CARE

• Treatment based on tumor location verses genomic drivers of disease

• Potential for more toxicity with less reliable treatment outcomes

PRECISION CANCER CARE

• Finding the right treatment for the right patient

• Potential for less toxicity with more reliable treatment outcomes
EMPIRIC CANCER CARE

• Treatment based on tumor location verses genomic drivers of disease

• Potential for more toxicity with less reliable treatment outcomes

Precision cancer diagnostics

Targeted therapy biomarkers
  - Kinase activation (EGFR, ALK, NTRK, etc.)
  - HRD biomarkers (BRCA1/2, ATM, etc.)

Immunotherapy biomarkers
  - PDL-1 IHC
  - Microsatellite instability
  - Tumor mutational burden

PRECISION CANCER CARE

• Finding the right treatment for the right patient

• Potential for less toxicity with more reliable treatment outcomes

Precision cancer care & precision cancer diagnostics
Precision cancer care & precision cancer diagnostics

**EMPIRIC CANCER CARE**
- Treatment based on tumor location versus genomic drivers of disease
- Potential for more toxicity with less reliable treatment outcomes

**PRECISION CANCER CARE**
- Finding the right treatment for the right patient
- Potential for less toxicity with more reliable treatment outcomes

**Precision cancer diagnostics**
- Targeted therapy biomarkers
  - Kinase activation (EGFR, ALK, NTRK, etc.)
  - HRD biomarkers (BRCA1/2, ATM, etc.)
- Immunotherapy biomarkers
  - PDL-1 IHC
  - Microsatellite instability
  - Tumor mutational burden

**Multi-drug chemo-immunotherapy**

**Single-agent precision therapies**
Molecular Diagnostics in Lung Cancer – Considerations and Relevance for Treatment Selection

Matthew Krebs, Clinical Senior Lecturer in Experimental Cancer Medicine, University of Manchester and Consultant in Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK
Traditionally lung cancer divided into histological sub-types

Pathologists are required to categorise lung cancer into adenocarcinoma and SqCC, because the same drugs used to treat adenocarcinoma can be inappropriate for treatment of SqCCs due to side effects, e.g. in the case of bevacizumab.

NSCLC: non-small cell lung cancer; SCLC, small cell lung cancer; SqCC, squamous cell carcinoma.

Understanding of genomic landscape of lung cancer has dramatically evolved in recent years.

### 2004
- **Adenocarcinoma**
  - KRAS: 25%
  - EGFR: 17%
  - Unknown: 35%
  - No driver detected: 12%

### 2014
- EGFR WT amp 1%
- EGFR exon 20 2.1%
- EGFR T790M 5%
- ALK 8%
- No driver detected 35%
- EGFR 4%
- KRAS 25%
- Other drivers 2.9%
- HER2 2%
- BRAF 2%
- PIK3CA 1%
- MET amp 1%
- NRAS 2%
- MEK1 <1%
- Two genes 4%

### 2017
- Sensitising EGFR 19.4%
- No driver detected 12%
- KRAS 25.3%
- EGFR WT amp 1%
- EGFR T790M 5%
- ALK Fusion 3.8%
- MET splice 3%
- Other drivers 2.9%
- ERBB2 2.3%
- BCR/ABL 2.6%
- ROS1 2.6%
- Other drivers 2.9%
- EGFR ex 20 2.1%
- BRAF V600E 2.1%
- PIK3CA 2%
- ALK Fusion 3.8%
- CDKN2A loss 1.9%
- RET Fusion 1.7%
- MET amp 1.4%
- ERBB2 amp 1.4%
- BRCA1/2 loss 1.3%
- BCR/ABL 2.6%
- TSC1/2 1.2%
- PTEN loss 0.7%
- MAP2K1 0.7%
- FGFR1/2 0.7%
- No mutation 1.2%
- TSC1/2 loss 0.7%

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1. [European Cancer Organisation](https://www.european-cancer-organisation.eu)
2. [European Cancer Organisation](https://www.european-cancer-organisation.eu)
3. [European Cancer Organisation](https://www.european-cancer-organisation.eu)
Advanced diagnostics inform therapy selection in lung cancer

**Targetable mutations in lung cancer**

- **EGFR**
  - sensitisising mutations: 17%
  - other 4%
  - sensitising 17%
  - other 4%
  - No oncogenic driver detected 31%
- **MET**
  - 7%
  - No oncogenic driver detected 31%
- **ALK**
  - 7%
  - No oncogenic driver detected 31%
- **ROS1**
  - 2%
  - No oncogenic driver detected 31%
- **RET**
  - 2%
  - No oncogenic driver detected 31%
- **NTRK**
  - 1%
  - No oncogenic driver detected 31%
- **BRAF**
  - other 17%
  - No oncogenic driver detected 31%
- **KRAS**
  - 25%
- **PIK3CA**
  - 1%
- **MEK1**
  - <1%

**Identifying actionable mutations with broad genomic profiling**


**Approved drugs**

- **EGFR**
  - Afatinib
  - Dacomitinib
  - Erlotinib (+anti-VEGF / VEGFR)
  - Gefitinib
  - JNJ-372
  - Necitumumab ▼
  - Osimertinib
  - Poziotinib
  - TAK-788
  - U3-1402
- **ALK**
  - Alectinib
  - Brigatinib
  - Ceritinib
  - Crizotinib
  - DS-6051b
  - Lorlatinib
  - Repotrectinib
- **MET**
  - Cabozantinib
  - Crizotinib
  - Capmatinib
  - Savolitinib
  - Tepotinib
- **HER2**
  - Afinatinib
  - Dacomitinib
  - Pertuzumab + trastuzumab
  - Poziotinib
  - TAK-788
  - Trastuzumab emtansine / deruxtecan
- **BRAF**
  - Dabrafenib (+ trametinib)
  - Vemurafenib
- **ROS1**
  - Copanlisib
  - Vemurafenib
- **PIK3CA**
  - Cobimetinib
  - Selumetinib
  - Trametinib
  - Vandetanib
- **MEK1**
  - Alectinib
  - Brigatinib
  - Ceritinib
  - Crizotinib
  - Ensicartinib
  - Lorlatinib
  - Repotrectinib
  - Selumetinib
  - Trametinib

**Investigational drugs**

- **EGFR**
  - Afatinib
  - Dacomitinib
  - Erlotinib (+anti-VEGF / VEGFR)
  - Gefitinib
  - JNJ-372
  - Necitumumab ▼
  - Osimertinib
  - Poziotinib
  - TAK-788
  - U3-1402
- **ALK**
  - Alectinib
  - Brigatinib
  - Ceritinib
  - Crizotinib
  - DS-6051b
  - Lorlatinib
  - Repotrectinib
- **MET**
  - Cabozantinib
  - Crizotinib
  - Capmatinib
  - Savolitinib
  - Tepotinib
- **HER2**
  - Afinatinib
  - Dacomitinib
  - Pertuzumab + trastuzumab
  - Poziotinib
  - TAK-788
  - Trastuzumab emtansine /
  - deruxtecan
- **BRAF**
  - Dabrafenib (+ trametinib)
  - Vemurafenib
- **ROS1**
  - Copanlisib
  - Vemurafenib
- **PIK3CA**
  - Cobimetinib
  - Selumetinib
  - Trametinib
- **MEK1**

All drugs listed are included in NSCLC NCCN Guidelines unless otherwise indicated. Some drugs are investigational and not approved in any indication. Some non-investigational drugs are only approved for use in specific indications in Europe and/or USA and/or Japan. Therapies marked with ▼ are subject to additional monitoring. Reporting suspected adverse reactions after authorisation of the medicinal product is important. Adverse events should be reported to your respective local office. Amgen Europe B.V.: Trastuzumab (Kanjinti); AstraZeneca AB: Osimertinib; Bayer AG: Lorlatinib; Celtrion Healthcare Hungary Kft.: Trastuzumab (Herzuma); Eli Lilly Nederland B.V.: Necitumumab; Eisai Europe Limited: Lenvatinib; Genzyme Europe B.V.: Vandetanib; Incyte Biosciences Distribution B.V.: Ponatinib; Ipsen Pharma: Cabozantinib; Mylan S.A.S.: Trastuzumab (Ozivir); Novartis’s Europharm Limited: Ceritinib; Pfizer Europa MA EEE: Trastuzumab (Trastraz); Pfizer Europe: MA EEE: Dacomitinib, Lorlatinib; Roche Registration GmbH: Alectinib, Cobimetinib; Samsung Bioepis UK Limited: Trastuzumab (Ontruzant); Takeda Pharma A/S: Brigatinib. 1. Adapted from Tsao, A.S., et al. (2016) J Thorac Oncol 11:613-38; 2. NSCLC NCCN Guidelines Version 2.2020; 3. NCT02609776; 4. NCT03260491; 5. NCT03271613; 6. NCT03318939; 7. NCT03693339; 8. NCT03693339; 9. NCT03693339; 10. NCT03778229; 11. NCT02664992; 12. NCT02465060; 13. NCT03855270; 14. NCT03505710; 15. NCT03426850; 16. NCT04209228; 17. NCT03206931.
Clinical guidelines do not always match clinical practice

**Biomarker testing in non-small cell lung cancer**

- **Key recommended tests**
- **Recommended to be assessed if NGS is used for broader testing**

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<th>Molecular testing method</th>
<th>Point mutations and small indels</th>
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<th>Rearrangements</th>
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<td>IHC</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>NGS (amplicon-based)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>NGS (hybrid capture-based)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

**Molecular testing guideline**

"In general, capture-based [NGS] methods may be preferable for initial testing of lung cancer samples in order to detect rearrangements... as well as a broader range of potential genetic markers"¹

"If available, multiplex platforms (NGS) for molecular testing are preferable"²

**ASCO Educational Book³**

**Biomarker testing for advanced NSCLC**

"For very limited samples... for which multiple tests cannot be performed, [hybrid capture-based] assays are preferable for upfront comprehensive assessment"

---

* IHC is used to detect MET overexpression and ALK translocations respectively.


Clinical guidelines do not always match clinical practice

**Biomarker testing in non-small cell lung cancer**

### Molecular testing method

<table>
<thead>
<tr>
<th>Point mutations and small indels</th>
<th>Copy number alterations</th>
<th>Rearrangements</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR and conventional sequencing</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>FISH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IHC</td>
<td>✓</td>
<td>✓</td>
</tr>
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<td>NGS (amplicon-based)</td>
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</tbody>
</table>

### CAP / IASLC / AMP¹ / ESMO²

**Molecular testing guideline**

"In general, capture-based [NGS] methods may be preferable for initial testing of lung cancer samples in order to detect rearrangements... as well as a broader range of potential genetic markers"¹

"If available, multiplex platforms (NGS) for molecular testing are preferable"²

### ASCO Educational Book³

**Biomarker testing for advanced NSCLC**

"For very limited samples... for which multiple tests cannot be performed, [hybrid capture-based] assays are preferable for upfront comprehensive assessment”

---


* IHC is used to detect MET overexpression and ALK translocations respectively.

Next generation sequencing – analysis and bioinformatics

Hybrid capture-based next-generation sequencing (NGS) identifies clinically relevant genomic alterations in a sample

Data aggregation and analysis allow translation of NGS information into actionable knowledge

Scientific/clinical expert review further aids clinical decision making

A curated, quality-controlled report aims to help physicians identify targeted or immunotherapy treatment options

Tissue versus liquid biopsy testing for genomic alterations

Tissue based genomic profiling remains standard of care with advantages such as higher sensitivity for certain types of alterations but suffers from limitations impacting patient care.

Patient care plan may suffer if timely testing not available, leading to reduced therapy options with potential higher adverse events.

The potential clinical applications of liquid biopsy are wide-ranging

- **Screening**
- **Diagnosis & prognosis & prediction**
- **Residual disease**
- **Recurrence**
- **Therapy selection**
- **Therapy response & resistance monitoring**

**Early cancer detection**

**MRD**

**Recurrence surveillance**

**Tx response monitoring**

- **Surgery**
- **Response to Neo Adj. therapy**
- **Mutations that arise early during tumor evolution**
- **Minimal Residual Disease (MRD)**
- **Recurrence**
- **Progression**
- **Therapy selection (CGP)**
- **1st line**
- **2nd line...**
- **Levels of ctDNA**
- **Time**

Immunotherapy is well established in advanced lung cancer

Timeline of developments for immunotherapies in lung cancer

Dependent on PD-L1 expression
Independent of PD-L1 expression

Pembrolizumab, 2L+2
mNSCLC*

Pembrolizumab, 1L6
Combination therapy
nonsquamous mNSCLC†

Nivolumab, 3L+7
mSCLC

Pembrolizumab, 1L11
Certain stage III or mNSCLC†

Atezolizumab, 1L13
Combination therapy
Nonsquamous mNSCLC†

Atezolizumab, 1L15
Monotherapy; mNSCLC†

2015
Nivolumab, 2L+3
mNSCLC*
Nivolumab, 2L+1
Squamous mNSCLC

2016
Pembrolizumab, 1L5
Metastatic NSCLC†
Atezolizumab, 2L+4
mNSCLC*

2017
Nivolumab +
Ipilimumab, 1L14
mNSCLC

2018
Atezolizumab, 1L9
Combination therapy
Nonsquamous mNSCLC†

2019
Atezolizumab, 1L10
Combination therapy
Extensive-stage SCLC

2020
Pembrolizumab, 1L8
Combination therapy
Squamous mNSCLC

Timeline:
- 2015: Nivolumab, 2L+3 mNSCLC*
- 2016: Pembrolizumab, 1L5 Metastatic NSCLC†
- 2017: Nivolumab + Ipilimumab, 1L14 mNSCLC
- 2018: Atezolizumab, 1L9 Combination therapy Nonsquamous mNSCLC†
- 2019: Atezolizumab, 1L10 Combination therapy Extensive-stage SCLC
- 2020: Pembrolizumab, 1L8 Combination therapy Squamous mNSCLC
BFAST: blood-first assay screening trial measures bTMB to inform clinical decision making in NSCLC

Screening inclusion / exclusion criteria*

- Age ≥ 18 years
- Unresectable, Stage IIIB or IV NSCLC
- Measurable disease
- Treatment naïve
- PS 0-2

ctDNA CGP testing (FACT CDx)

Sample (+) for BFAST alteration

Physicians will receive overall results from bSMP assay

Sample (-) for BFAST alteration

ctDNA CGP testing (FACT CDx)

ALK+

Alectinib

RET+

Alectinib

bTMB+

Atezolizumab

Platinum-based CTx

ROS1+

Entrectinib

Real World Data Cohort

Physicians will receive overall results from bSMP assay

*All cohorts have additional, treatment-specific inclusion / exclusion criteria


Phase II/III BFAST trial1

- Treatment-naïve, aNSCLC patients screened using blood-based NGS assays and enrolled into targeted treatment / immunotherapy cohorts
  - Median bTMB at baseline was 2 mutations
  - 3/87 (3.4%) had bTMB ≥ 16 mutations
  - LBx identified a similar proportion of patients with ALK mutations (5.4%) to that typically seen with traditional biopsy (5%)
  - 12-month DoR was 75.9%
Conclusions

- Lung cancer is the poster boy for precision medicine with effective targeted treatments licensed and in development.

- Liquid biopsy is convenient, efficient and technologies have evolved to perform broad panel testing from ctDNA.

- Tissue testing for NGS still has its place and will likely be complementary with liquid-based testing.

- Serial sampling provides important insights into potential resistance mechanisms and will guide next generation of targeted therapies.

- Challenges will be funding of NGS in different health-care systems and reimbursement of therapies.

**How to integrate these advanced diagnostics tools into clinical routine?**
Open Discussion

Please use the Chat feature to ask questions and make comments
Final Remarks

Co-Chair:

Geoff Oxnard, Vice President, Global Medical Lead, Liquid Franchise at Foundation Medicine
Removing health system delays in lung cancer

Co-Chair: 
Ouzna Morsli, EMEAC Oncology Medical Lead, MSD
Time is of the essence for people living with lung cancer: delays in diagnostic testing and referral for treatment must be eliminated.
Removing health system delays in lung cancer

The Dutch Lung Cancer Audit: Nationwide Quality of Care Evaluation Using Quality Indicators

Hans J.M. Smit, Pulmonologist, Rijnstate Hospital, Chairman of the Dutch Lung Cancer Audit, Arnhem, The Netherlands

Rawa Ismail, PharmD and PhD Candidate DICA
What to achieve

- Improving quality by benchmarking
- Preferably in a safe setting (anonymous)
Key messages

- Quality registries play an important role in quality care improvement
  - It takes time to initiate a nation-wide registry
  - Insight into own data leads to improved care
  - Benchmarking with other hospitals can lead to discussions and best-practice examples

- Quality indicators are important to measure the quality of care: start “simple”, improve over time
  - Be aware of the registration burden for hospitals
  - Indicators on processes in the hospital can lead indirectly to better care
  - Outcome indicators are of high value and should be measured when registry data are rich and trustworthy
• What is DLCA?
• How was DLCA initiated?
• What is measured?
• What has been achieved?
• How to use it in clinical practice?
Multidisciplinary DLCA within DICA

2009
Start DICA:
Dutch ColoRectal Audit (DCRA)

2012
Start Lung surgery (DLCA-S)

2013
Start Radiotherapy (DLCA-R)

2015
Start Cardio-Thoracic surgery (DLCA-S)

2016
Start Lung Oncology (DLCA-L): one DLCA
The DLCA-L

First results DLCA-L published

Codman dashboards live: benchmark information

Start DLCA-L by Medical Association

Outcome indicators (survival), automatic data retrieval...

Impact on patients quality of life

2016

2018

2020

2021
DLCA board

Mandated from Specialists Association and Patient Representatives

- Open character
- Publications
- Develop Indicators:
  - Based on guidelines
  - Based on science
  - Based on patient needs

DICA

Scientific bureau

Based on guidelines
Based on science
Based on patient needs

DICA supports law, ICT, epidemiology

Finance by production payment

Hospital 1
Hospital 2
Hospital 3
Hospital 4
Hospital 5

Finance by government

DICA through MRDM

Finance by government

Scientific board
Initiation of DLCA

- Initiated by professional association of chest physicians (NVALT)
- Facilitated by DICA
- Subregistries with own scientific committees and clinical audit board
DLCA-L >40,000 patients
73 hospitals

DLCA-S >42,000 patients
43 hospitals

DLCA-R >18,000 patients
19 hospitals
Initiation of the DLCA

Why?

Insights into quality of care of lung cancer patients

by focusing on

• Diagnostics
• Time to Diagnosis and Therapy
• Monitoring of in-hospital times,
• Outcomes of systemic therapy
• Including Best Supportive Care = complete
Potential problems

Registration = time consuming
Time = competitive with patient care
Automic substraction = less control

Privacy law = reduction of possibilities and time consuming
The DLCA dataset

- Inclusion: all patients with lung carcinoma
- Including clinically suspected
- 153 variables
- >40% mandatory items
Results: Data set completeness
Results: Hospitals and immunotherapy
Results: Numbers of patients per hospital
Results: Feedback process

The Audit Cycle

- Identify audit topic
- Implement change
- Set standard
- Collect data
- Data analysis

Ernest Amory Codman, 1910
Results: Quality indicators

1) Structure quality indicators
   - Number of patients
   - Completeness of registration

2) Process quality indicators
   - Brain imaging
   - Molecular diagnostics
   - Multidisciplinary consultation
   - Duration diagnostic trajectory
   - First-line treatments NSCLC/SCLC
   - Use of treatments in elderly

3) Outcome quality indicators
   - Grade 3/4 toxicities related to systemic treatment
Results: Improvement in brain imaging

2017

2019
Results: Other examples of QIs

- Stage III NSCLC patients undergoing brain imaging:
  - 82% in 2017 → 90% in 2019

- Stage IV adenocarcinoma patients undergoing molecular diagnostics:
  - 89% in 2017 → 93% in 2019

- Time from diagnosis to start treatment
  - Without invasive mediastinal diagnostics (<21 days): 62%
  - With EUS/EBUS (<21 days): 46%
  - With mediastinoscopy (<35 days): 59%
Use in clinical practice

DLCA
DUTCH LUNG CANCER AUDIT

shared decision making
Information and recommendations

Clinician

Values and preferences

Patient
<table>
<thead>
<tr>
<th>Leeftijd ten tijde van diagnose</th>
<th>Amount</th>
<th>Your health facility</th>
<th>Your health facility SD</th>
<th>Benchmark NL</th>
<th>Benchmark NL SD</th>
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<tbody>
<tr>
<td></td>
<td>61</td>
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<td>10.6</td>
<td>69.5</td>
<td>10.1</td>
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<table>
<thead>
<tr>
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<th>Amount</th>
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<th>Benchmark NL</th>
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<tr>
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<td>&gt; 80 jaar</td>
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<td>14.6 %</td>
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<table>
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<th>Amount</th>
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<td>53.8 %</td>
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<td>Vrouw</td>
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<tr>
<td>Onbekend / niet ingevuld</td>
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<td>–</td>
<td>1.4 %</td>
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<table>
<thead>
<tr>
<th>ECOG score</th>
<th>Amount</th>
<th>Your health facility</th>
<th>Benchmark NL</th>
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<tbody>
<tr>
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<td>3</td>
<td>4.8 %</td>
<td>13.5 %</td>
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Key messages

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Thank you!

Raw Ismail
r.ismail@dica.nl
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Final Remarks

Co-Chair:
Ouzna Morsli, EMEAC Oncology Medical Lead, MSD
Legacy from this meeting will include:

- Action report to be published in early January
- From tomorrow, video and slides on our website: [europeancancer.org/resources](http://europeancancer.org/resources)
- Follow up with EU Commission ahead of publication Europe's Beating Cancer Plan
- Next steps on implementation of Essential Requirements in our Quality Cancer Care Network
All the sessions from this year’s European Cancer Summit are now available free of charge on wondrmedical.net/ch/european-cancer-organisation
Quality Cancer Care Catalogue

• The European Quality Cancer Care Catalogue aims to provide a central repository to signpost individuals to the tools they will find helpful in improving the quality of cancer care.

• The Catalogue is a continually evolving home for societies and other entities to profile and disseminate their work to broad audiences likely to have interest in their initiatives.