IMPROVING THE USE OF EGFR MUTATION TESTING IN ADVANCED NON-SMALL CELL LUNG CANCER –

INSIGHTS FROM AROUND THE WORLD
EGFR Mutation Testing and Treatment Considerations in Advanced Non-Small Cell Lung Cancer

Introduction – Dr Matthew Peters, Macquarie University Australia and Global Lung Cancer Coalition

Purpose of this insights report

Lung cancer, mutation testing and treatment considerations

Expanding our knowledge about EGFR testing in advanced non-small cell lung cancer

A Focus on Europe

Germany

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Spain

UK

Case study: France

A Focus on North America

Canada

US

What’s Next?

Working together for equitable access to personalised testing and treatment

Acknowledgements

References
INTRODUCTION –
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EGFR MUTATION TESTING AND TREATMENT CONSIDERATION IN ADVANCED NON-SMALL CELL LUNG CANCER

PURPOSE OF THIS INSIGHTS REPORT:

As chair of the Global Lung Cancer Coalition, I am all too aware of the disparities in diagnosis and care of lung cancer across the world. To help contextualise the similarities, differences and barriers in daily practice across countries, this insights report has been compiled using real-life perspectives from those working on the ground in lung cancer; healthcare professionals and patient organisations. Their qualitative insights build on the foundation of findings garnered from a recent international survey of lung cancer oncologists and respiratory experts about advanced non-small cell lung cancer (NSCLC), see later section.

Ultimately, the shared vision of healthcare professionals, societies and patient organisations around the world is to optimise clinical practice in all regions to ensure every person with NSCLC receives an early diagnosis, the necessary tests, and appropriate treatment based on their individual personal and medical circumstances, and the characteristics of their lung cancer, to help them achieve the best outcome for them in terms of length and quality of life. Differential health care resourcing is the reality across the world and will remain so for the reasonably foreseeable future, but it should be a common expectation that resources available are used optimally.
LUNG CANCER IS THE MOST COMMON CAUSE OF CANCER DEATHS WORLDWIDE, CLAIMING 1.59 MILLION LIVES IN 2012 – CONSIDERABLY MORE THAN CANCER OF THE LIVER, STOMACH, COLON AND BREAST.1

Non-small cell lung cancer (NSCLC) is the most common form of lung cancer,2 which accounts for 80-85% of all lung cancer cases.3 There are three main types of NSCLC (adenocarcinoma; squamous cell carcinoma; large cell carcinoma).2 Often, lung cancer is diagnosed at a late stage (‘advanced’) which can make it even more difficult to treat.4 Upon diagnosis of NSCLC, in addition to the stage of the cancer, various factors can have an impact on the treatment options available to each individual, including the individual’s general health, and if the cancer has mutations in certain genes.5

The Epidermal Growth Factor Receptor (EGFR) gene is found at abnormally high levels in many types of cancer cells. More importantly in lung cancer, mutations in this gene have been identified that can drive tumour growth and create an opportunity for treatment intervention. A ‘mutation test’, sometimes referred to as a genetic / gene test, can be used to identify if one of these gene mutations is present. EGFR mutations are found in 10-15% of Caucasian and 40% of Asian patients with NSCLC.6 There are different types of EGFR mutations; the most common, which account for 80–90% of all EGFR mutations, being delE9 and L858R.7
International guidelines recommend that EGFR mutation testing should be performed at diagnosis of advanced stage NSCLC (adenocarcinoma type), and that these test results should guide treatment decisions to ensure the right treatment is given according to the cancer and mutation type. This is important as recent data has shown that tailoring treatment according to mutation type could improve a person’s quality of life and potentially extend length of life (overall survival).

Despite recommendations from international guidelines, carrying out EGFR testing upon diagnosis of advanced NSCLC (adenocarcinoma) varies greatly in clinical practice across regions. Asia is leading the way boasting the highest rates of testing (92%) compared to Europe and the US (77% and 76% respectively). A possible explanation for these high levels of testing rates in Asia could be due to the high rates of EGFR mutations amongst Asian populations. However even when EGFR testing is carried out to detect an individual’s mutation subtype, often doctors do not wait for the test results before making treatment decisions (30% in Europe; 26% in the US; 12% in Asia), signalling that many people with advanced NSCLC are not receiving personalised treatments for their cancer and mutation type.
In a quest to better understand the NSCLC landscape, a recent international survey set out to assess the prevalence of EGFR mutation testing, identify barriers to testing, uncover oncologists’ and respiratory experts’ (pulmonologists in France, Germany, and in Asian countries; thoracic surgeons in Japan) attitudes towards testing, and to better understand how test results affect their therapy considerations.

**METHODOLOGY**

An online survey was conducted in 10 countries (Canada, France, Germany, Italy, Japan, South Korea, Spain, Taiwan, UK and US) involving 562 healthcare professionals who treat people with advanced NSCLC who have an EGFR mutation (also known as EGFR mutation-positive). The survey took place from December 2014 - January 2015.
SUMMARY OF FINDINGS

HEALTHCARE PROFESSIONALS ARE UNDERUTILISING PERSONALISED TREATMENTS FOR PEOPLE WITH ADVANCED EGFR MUTATION-POSITIVE NSCLC

- EGFR mutation testing rates were high for newly diagnosed patients (81%) but rates varied between regions.
- For nearly one in four patients tested for EGFR mutations, results were not available in time to guide treatment decisions – with significant differences between regions (range: 12% in Asia to 30% in Europe).
- Half of healthcare professionals surveyed (51%) reported that their treatment decision was not guided by a patient’s EGFR mutation subtype – again with significant differences between regions (range: 28% in Asia to 60% in Europe).
THE FINDINGS FROM THIS INTERNATIONAL SURVEY OF HEALTHCARE PROFESSIONALS HIGHLIGHT CLEAR VARIATIONS IN HOW ADVANCED NSCLC IS TREATED IN CLINICAL PRACTICE BETWEEN THE REGIONS SURVEYED.

As lung cancer is so common and the biggest cancer killer, if patients receive suboptimal care this poses a major worldwide problem. If we were to equate this to invasive bowel cancer, for example, this would mean not a single patient would be treated in accordance with best practice. NSCLC diagnosis, mutation testing (for adenocarcinoma type) and associated treatment guidelines are of high importance to extend a person’s quality of life and overall survival, therefore continuing healthcare professional education could be one important aspect to address the barriers and regional discrepancies which have been identified.

BARRIERS TO EGFR TESTING VARIED BETWEEN REGIONS

The main reasons for not testing all patients, aside from tumour histology, were:

- Insufficient tissue / uncertainty of sufficient tissue to perform the test
- Poor general health (performance status)
- Long turnaround time of the results

TREATMENT CHOICES:

Almost 1 (24%) in every 4 patients were started on first-line treatment before test results were available

AND

1/2 OF ONCOLOGISTS reported their treatment decision was not affected by a patient’s EGFR mutation subtype

OVERALL LEARNINGS
“National guidelines in Germany strongly recommend EGFR mutation testing before starting first-line therapy – however in clinical practice there are some shortfalls. A number of factors are impacting testing rates in Germany, which include a lack of reimbursement for testing inpatients, despite more than 95% of patients with lung cancer diagnosed in an inpatient [i.e. hospital] setting; not having an agreed national testing rate to work towards; and the speed and efficiency of test results. More pressure needs to be placed on the healthcare system to revise its reimbursement approach, in order to allow all patients eligible for mutation testing to receive it. A cure is the ultimate goal for advanced NSCLC, however until this becomes a reality, the right treatment should be given to the right patients early, to help with both their quality of life and overall survival rates.”

PROF. DR. MED.
FRANK GRIESINGER,
M.D., Ph.D.
Chief of the Department of Hematology and Oncology, Pius Hospital Oldenburg, Cancer Center, Oldenburg, Germany
GERMANY

“Insufficient reimbursement for inpatients is a big barrier in Germany, which is currently limiting access to EGFR testing for many eligible patients with advanced NSCLC. Molecular testing is not adequately represented within the DRG-system – Germany’s pricing structure for hospital services – so this needs tackling head-on in order to achieve meaningful change for patients across the country in how their condition is treated. And when molecular testing is carried out, results can take up to 2 months to reach a physician, so the practicalities and processes need evaluating.”

DR. MARKUS TIEMANN, Founding Partner and Managing Director of the Institute of Hematopathology, Hamburg, Germany

ITALY

“In Italy a significant number of patients with lung cancer are tested for EGFR mutations, but there are some patients (and caregivers) who ask to start first-line treatment immediately without waiting for test results. I believe that some crucial points should be underlined for the benefit of patients: today we have targeted therapies available for some forms of lung cancers, EGFR-mutation cases being an example, which benefit from a specific treatment upon diagnosis. It’s essential that all necessary elements to select the most appropriate therapy are collected before starting treatment, which we understand is difficult for patients and caregivers to understand given their anguish in that moment of diagnosis. It’s necessary to wait for all tests to be performed, which today in Italy take on average one week to complete.”

PROF. SILVIA NOVELLO, President of WALCE (Women Against Lung Cancer in Europe), Italy
“EGFR testing rates in Spain have been consistently high for a long time, which has been helped by educational programmes and adopting a multidisciplinary approach to testing. A national programme for EGFR testing is currently being implemented across the country. However, the two biggest challenges which healthcare professionals must contend with are availability of tissue samples, and turnaround time of testing results. If these two key factors are addressed, this could improve testing rates to ensure more eligible patients receive personalised medicine that is best suited to them.”

DR. ROSARIO GARCÍA CAMPELO, Medical Oncologist, Complejo Hospitalario Universitario A Coruña, Spain

NATACHA BOLAÑOS, Cancer Rehabilitation Specialist, Patients & Public Affairs, Spanish Group of Cancer Patients / Grupo Español de Pacientes con Cáncer (GEPAC), Spain

“Over recent years, the approach to lung cancer management in Spain has seen multiple changes, particularly since genetic testing has become a standard process. Today, Spain stands out in personalised treatment of lung cancer. In most Spanish cancer centres, EGFR testing rates are high and results are accessible in a suitable timeframe. However, with the growing economic crisis, there is increasing concern that some centres are neither able to carry out testing directly, nor send samples to other centres or laboratories, which can result in access inequality for some people who are eligible to receive EGFR testing. The ideal situation is a challenging one; to achieve a coordinated approach amongst all hospitals, cancer centres and laboratories across Spain, supported by a national health care system. Laboratories and centres of all sizes need access to innovative technologies in order to carry out EGFR testing, and the turnaround time of results needs to be optimal to inform therapy choices. We need to stop short-term thinking which is strictly financially led, because this often leads to higher costs in the long-term.”
“Despite high levels of EGFR mutation testing in the UK, some patients start treatment for advanced NSCLC before results of this testing are available. In addition, some do not receive treatment personalised for their mutation subtype, even though evidence shows this may improve overall survival. This international survey of EGFR testing found, for instance, that more than one in five UK patients with advanced NSCLC do not receive treatment personalised for their mutation, suggesting that implementation of UK guidelines is not complete. There is therefore still work to be done, and a first step is to discover what barriers stand in the way of compliance with established guidelines.”

DR JAMES SPICER, of King’s College London, at Guy’s Hospital, London, UK

“We have to recognise the achievements made over recent years with regards to the availability of EGFR testing in the UK. We’ve come a long way; from no testing, to now being in a great position where the majority of patients have access to these diagnostic tests. The key challenges we face however, include turnaround time of test results; and the availability of tissue samples in order to carry out these tests. Working with the pathology service, a crucial player in this discussion, we need to find practical solutions to overcome these barriers in order to ensure EGFR testing features as part of a standardised treatment pathway for all patients – whether they are informed patients who actively seek testing from their healthcare team, or patients who prefer not to proactively enquire about their disease or treatment pathway. Lung cancer remains the UK’s biggest cancer killer, and the battle continues. We need to do all we can to help those affected by this disease, for today as well as for tomorrow – which is a continuing challenge given the general population is living longer, and lung cancer is typically seen in higher levels amongst the older generation.”

DR JESME FOX, Medical Director, The Roy Castle Lung Cancer Foundation, UK
Equal access to personalised cancer treatment is essential from a public health perspective, and in 2006 in France, the French National Cancer Institute (INCa) and the French Ministry of Health set up a national network of 28 regional molecular genetics centres to help achieve this vision.

In these dedicated centres, genetic tests are carried out free of charge for people diagnosed with cancer who require testing, irrespective of where they are receiving their treatment in France.

In 2010, the national molecular genetics network launched a programme specifically aimed at people with specific types of cancer, including lung cancer. The programme aimed to detect emerging biomarkers (biological/genetic features) in preparation for new targeted therapies under development, to help ensure a fast response to testing when/if these would become approved. For lung cancer, this included EGFR mutation testing. More than 65,000 people in France with various cancers underwent genetic ‘predictive’ tests in 2013. France is the first country in the world to have nationwide genetic testing to this extent with at least five years data/experience.

In 2013, the national molecular genetics network carried out EGFR mutation testing for 23,336 people. This resulted in the identification of 2,333 people (10%) with an EGFR mutation, making them eligible for targeted treatment.
"In Canada, the healthcare system is publicly funded through each province and territory. To ensure EGFR testing is offered at diagnosis to all eligible patients across the country, there is a need for national policy standards and a sustainable public funding model for testing. As lung cancer treatment evolves, mutation testing increasingly dictates therapy, so this is an essential part of the process. Each and every eligible patient across Canada therefore needs to be diagnosed, tested and treated in a timely fashion, now and in the future.”
In the United States, a substantial percentage of treatment decisions are not based on EGFR mutation subtype and as a result lung cancer patients are not receiving personalized treatment plans. Determining EGFR mutation status is a critical prognostic factor that should be adopted to determine the most appropriate treatment options for patients. One would not start a patient with breast cancer on treatment without knowing hormone receptor or HER2 status. We must be diligent in testing appropriate patients for mutation status to offer the most appropriate therapy.

Physician education and clear guidelines are two of the biggest barriers in the United States which are currently holding back eligible patients with advanced NSCLC from receiving EGFR mutation testing. This is particularly so within the community setting, where the majority of patients are treated. The landscape of how to diagnose and treat lung cancer is changing rapidly, and as a result, we need a more efficient way to get the information to the general oncologist; and also in tandem, help educate the public about the importance of molecular testing. We need to do more to ensure that EVERY patient is tested. The right drug needs to get to the right patient, at the right time.
WHAT’S NEXT?

WORKING TOGETHER FOR EQUITABLE ACCESS TO PERSONALISED TESTING AND TREATMENT

COUNTRY-LEVEL PERSPECTIVES OUTLINED WITHIN THIS INSIGHTS REPORT DO VARY, HOWEVER THERE IS AN OVERARCHING COMMONALITY; A SHARED VISION THAT EXISTS AT AN INTERNATIONAL AND NATIONAL LEVEL TO ENSURE EVERY PERSON WITH NSCLC RECEIVES THE RIGHT DIAGNOSIS AND TESTS NEEDED, SO THEY CAN HAVE ACCESS TO THE MOST SUITABLE TREATMENT FOR THEM.

Guidelines mirror this notion with strong recommendations for mutation testing to be undertaken before treatment is commenced in people with NSCLC (adenocarcinoma). Personalised medicine holds great promise, however it also poses a host of challenges before it can become standardised in clinical practices across a nation; let alone across regions.

Certain limitations are, however, currently holding many healthcare systems back from achieving standardised mutation testing for all who could benefit from it in their country, with common challenges seen across many countries – namely how to obtain adequate tissue samples and then achieve accuracy and reproducibility of mutation tests and analyses; how to speed up the analysis time of mutation test results in order to better inform treatment considerations; and how to ensure the testing process is sustainable for roll-out across an entire country.

Education is key for patients as well as for healthcare professionals – for the latter, best practice sharing within the medical community is important to continue to raise awareness of targeted treatments and associated mutation testing.

More is needed to ensure all who require education, resources and support receive it, bringing us one step closer to the vision that every person with NSCLC receives the best management possible to help them live a better length, and quality, of life.
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