The 3rd European Lung Cancer Conference

Highlights from the 3rd European Lung Cancer Conference (ELCC), 18-21 April 2012, Geneva, Switzerland

T. Feys

From April 18th till April 21st, the third European Lung Cancer Conference (ELCC) was hosted in Geneva. Over the past few years, the ELCC has become the reference event in Europe for professionals treating patients with lung cancer. The third edition of this exciting meeting provided a comprehensive multidisciplinary overview of the state-of-the-art knowledge in thoracic malignancies, covering different aspects such as prevention, screening, early diagnosis, treatment modalities and the result of translational and clinical research. The meeting attracted over 1,500 attendees from all over the world. This report does not pretend to summarise the entire meeting but simply aims at discussing some important take-home messages from the congress.

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Early detection techniques

Effectiveness of chest digital tomosynthesis for early lung cancer detection

A fast and inexpensive new imaging technique, called digital chest tomosynthesis, was shown to be a promising method for lung cancer screening. Bertolaccini et al. used the technique to screen over 1,500 patients with no previous evidence of cancer.[1] Abnormalities were found in the lungs of 268 subjects, of whom 16 (1.07%) were found to have lung cancer. This 1% lung cancer detection rate seen with digital chest tomography is in line with the detection rate of previous studies using computed tomography. However, digital tomography takes only 11 seconds and the cost is substantially lower than low-dose CT. Furthermore, compared to chest CT, patients undergoing digital chest tomography received a far lower radiation dose. As such, digital chest tomography seems to be a promising first-line tool for lung cancer screening. Further multicenter studies are needed to confirm the clinical role for the technique in the detection or evaluation of lung nodules.[1]

An artificial nose sniffs out cancer

Developed by Prof Haick and collaborators, the NA-NOSE detects volatile organic compounds in an individual's breath using an array of cross-reactive sensors, and then identifies patterns in the molecules allowing it to differentiate between the breath of healthy people and lung cancer patients. The aim of the presented study was to evaluate the role of exhaled breath as a potential non-invasive biomarker to distinguish between benign and cancerous conditions, which might be used prior to biopsy. In total, 74 participants with 'single pulmonary nodules' detected by imaging were included in the study. The NA-NOSE was 88% accurate in distinguishing between benign and malignant nodules, the

Authors: T. Feys MSc MBA, Ariez International, c/o PO Box 271, 1520 AG Wormerveer, The Netherlands, tel: +32 (0)479 567890, e-mail: t.feys@ariez.com.

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researchers report. The sensitivity of the test was 86% (correctly identified 86% of the malignant nodules) and its specificity was 93% (correctly identified 93% of the benign nodules).[2]

The ultimate goal of the NA-NOSE device is to identify the changes in the volatile biomarkers' concentrations allowing for early diagnosis of cancer in very early stages.

Only patients who test positive on this device should then require conventional, unpleasant and expensive invasive procedures to locate their tumour. As such, patients will go on to be treated in an early stage, when cure rates are much higher.[2]

Advanced non-small cell lung carcinoma

New analysis to guide erlotinib use in advanced non-small cell lung carcinoma

Results of the biomarker analysis of the phase III TORCH trial, which compared the efficacy of treatment with erlotinib, followed by cisplatin and gemcitabine at disease progression to the standard, reverse sequence, confirm that patients with unknown or negative EGFR mutation status should be treated with the standard chemotherapy first. Data from the TORCH-BIO study show a significant interaction in progression-free survival (PFS) favouring treatment with erlotinib first in EGFR-mutated patients and favouring chemotherapy first in EGFR-wid type patients. However, no significant interaction was seen between treatment efficacy and overall survival (OS).[3] This demonstrates that using erlotinib to treat an EGFR mutated tumour is always effective, both in first and second line. Of course, as shown in several other trials, it is much more convenient for these patients to receive it as first-line therapy. The take-home message from this study is that in advanced non-small cell lung carcinoma (NSCLC) patients, treatment with erlotinib first should only be applied to patients whose tumour is known to harbour EGFR mutation. Patients with unknown or negative mutation status should be treated with the standard chemotherapy first.[3] These conclusions join the now generally accepted proposal that only patients that carry an EGFR mutation should be treated with EGFR TKI's.

Of note, this biomarker analysis was preplanned, but actually only 36% of the samples could be analysed for EGFR mutation status. This relatively low tissue accrual rate is precedented by many clinical trials in which the mutation analysis was performed retrospectively.[3]

KRAS mutational status impacts PFS of NSCLC patients treated with platinum based chemotherapy

KRAS mutations in NSCLC are supposed to indicate a poor prognosis and poor response to anticancer treatment. However, such evidence is only drawn from retrospective series giving controversial results. In this light, a study was set up to prospectively assess the prognostic value of KRAS mutations in NSCLC patients treated with a first-line platinum-containing chemotherapy regimen. Patients mutated for KRAS demonstrated a significantly higher risk of progressing compared to KRAS wild type patients (HR[95%CI]: 1.42[1.06-1.94]; p=0.02). These results suggest that KRAS mutation epidemiology in this setting highly differs from that of colon cancer.[4]

Biomarkers guide lung cancer therapy

Gene signature identifies NSCLC patients with a higher risk of relapse

NSCLC often remains undiagnosed until it has grown and spread throughout the body. Even those patients who are diagnosed early enough to undergo surgical removal of the tumour still have a discouraging 30% rate of relapse.

Researchers hope that identifying which patients have the greatest risk of relapse will allow to focus other treatment strategies, in order to improve their chance of being cured after surgery. Researchers from Hospital Clinico San Carlos, Madrid, have found a 50-gene predictor that appears to be capable of doing just that. In a study of 84 patients with stage I and II NSCLC, who had undergone surgery to remove their tumour, the gene signature accurately predicted which patients were at low risk of relapse. The different genes of the predictor were over-expressed in roughly one-third of patients, all of whom had a low risk of relapse. Further analysis showed that these genes were related to the activity of B-lymphocytes. The fact that this B cell-dependent immune response was associated with a better outcome suggests that its therapeutic applications in the management of these patients after surgical resection should be investigated.[5]

MicroRNA marks response to chemoprevention

Research from Mascaux et al identified micro RNA miR-34c as a potential biomarker for histological response in lung cancer chemoprevention studies. Currently, the best intermediate endpoint for studies of chemoprevention is a histological grading of cells in the airways of the lungs. However, more quantitative biomarkers of response would be desirable. In this light, the expression of set of selected micro RNAs was evaluated in 125 former or current smokers enrolled in a chemoprevention trial that compared iloprost to placebo.[6]

After analysing 14 different micro RNAs from 496 lung biopsies, investigators found that a change in the expression of miR-34c in follow-up biopsies was inversely correlated with a histological response. As such, changes in the miR-34c expression may therefore be a quantitative biomarker of response in lung chemoprevention studies.[6]

Expression levels of ribonucleotide reductase subunit 2 predicts survival

In a study including 82 patients with stage I-III NSCLC, expression levels of ribonucleotide reductase subunit 2 (RRM2) were shown to predict shorter survival. The difference in OS between patients with high or low RRM2 levels was clinically relevant. The mean survival time of patients with high RRM2 levels was 36.5 months compared to 46.1 months for those with low RRM2 levels. The role of RRM2 as an unfavourable prognostic marker is in agreement with its crucial role in supplying deoxyribonucleotides for DNA synthesis and repair and with the finding that cells overexpressing RRM2 exhibit enhanced cellular invasiveness.[7]

A promising biomarker of response to radiotherapy

In a study from Trigonis et al, F-18 fluorothymidine (FLT), a tracer molecule used in PET scanning, was used to measure tumour cell proliferation. In this study, 14 patients with NSCLC received a total of 31 dynamic FLT PET-CT scans before and within 1-2 weeks after the start of radical radiotherapy. The investigators found that radiotherapy induced early significant decreases in tumour FLT uptake that varied across patients. These results indicate the potential of FLT PET to identify how well patients are responding to radiotherapy and guide therapeutic approaches.[8]

Promising developments in the management of mesothelioma

Micro RNAs speed-up the diagnosis of mesothelioma

At present, diagnosing mesothelioma depends on the availability of a lung biopsy containing enough tumour tissue. However, suitable biopsies are not always available, which may leave doctors uncertain about the patient's diagnosis, sometimes resulting in a delay to the start of treatment. So far, a number of proteins have been proposed as blood-based markers for malignant pleural mesothelioma; however, none of these has so far reached the accuracy required for routine clinical use. In a study presented by Kirschner et al, microRNAs in the blood were explored as potential diagnostic markers for mesothelioma. The study included five patients with malignant pleural mesothelioma and three healthy controls, and identified seventeen microRNAs with significantly differential expression in the two groups. In a second step, these miRNAs were validated in a series of blood samples from fifteen patients and thirteen controls.[9]

The study revealed that the level of miR-625-3p was four-fold higher in the blood of mesothelioma patients compared to healthy controls. Measuring levels of this miRNA blood samples allowed the researchers to discriminate between mesothelioma patients and controls with an accuracy of 82.4%. Further studies on larger sample sizes are needed to see whether the accuracy of miR-625-3p can be confirmed or even turn out to be better than currently observed.[9]

High-dose radiotherapy gives good response rates in mesothelioma

Despite the widespread belief that mesothelioma does not respond to radiotherapy, researchers reported at ELCC that it may have the best response rates of any single treatment for patients with mesothelioma largely confined to one side of the chest.[10] Between 2003 and 2011, Feigen et al gave radiotherapy to 45 patients aged 45-74 with doses between 45 and 60 Gy to one side of the chest over six weeks. The radiation was administered using 3D-conformal or intensity-modulated radiotherapy. None of the patients underwent surgery to remove the affected lung. At the beginning of treatment more than 80% of patients had the more advanced stage III or IV disease, and all but two received prior chemotherapy and/or surgery.[10]

The median survival for the patients was 12.4 months from starting radiotherapy, ranging from 2-87 months, the researchers reported. Furthermore, no life-threatening or fatal toxicities from treatment were observed. This study provides clear evidence that radiation is arguably the most effective single agent for mesothelioma and new technologies including intensity-modulated radiotherapy allow high doses to be delivered safely.[10]

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