INTERVIEW

Interview: developing therapies for lung cancer

Silvia Novello* speaks to Roshaine Wijayatunga, Managing Commissioning Editor: Silvia Novello is a Full Professor of Medical Oncology in the Oncology Department at San Luigi Hospital in Orbassano, Italy, part of the University of Turin. She earned her medical degree and completed the postgraduate training in respiratory medicine and medical oncology at the University of Turin and partially at the Institut Gustave Roussy in France. Currently, she is head of the Thoracic Oncology Unit at the San Luigi Hospital, Orbassano (Turin), where she also tutors medical students and postgraduate students in respiratory medicine and medical oncology. Novello’s research interests include thoracic malignancies, primary prevention, gender differences in lung cancer, basic and clinical applied research on lung cancer, including pharmacogenomics. She is involved in many European and national controlled clinical trials evaluating new approaches in diagnosis and lung cancer therapy.

From July 2012 until 2016, Novello has been a Member of the Board of Directors of the International Association for the Study of Lung Cancer and since October 2016 Member of the Board of Directors of the Italian Association of Medical Oncology and member of other several scientific societies including the American Society of Clinical Oncology and the European Society of Medical Oncology. Currently, she is the President of Women Against Lung Cancer in Europe, a nonprofit European Association founded in 2006 in Turin, Italy, part of the scientific Committee of Lung cancer Europe and also a member of the Scientific Committee of Bonnie J Addario Lung Cancer Foundation and Member of the Scientific Committee of Investigación sobre Cáncer de Pulmón en Mujeres. She is the author or co-author of over 100 publications in peer-reviewed journals.

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What led you into lung cancer research?

I started my career as a Pulmonologist and my major interest was thoracic oncology since the beginning. This was mainly due to the possibility to merge clinic and research. Having this background is somewhat easier to deal with these patients, who are frequently heavy smokers (or former smokers), with comorbidities that are part of the daily clinical practice for a Pulmonologist.

You have been involved in the AURA study. Could you tell us a little about the aims & findings of the study?

The AURA trials are another important piece in the thoracic oncology field looking...
first at the safety and activity of osimertinib in EGFR-mutated patients and also to its efficacy compared with chemotherapy in progressing advanced/metastatic EGFR T790M mutation-positive NSCLC patients who have received prior EGFR TKI therapy. This drug is approved by US and European regulatory agencies and recommended in national and international Guidelines, being currently the treatment for those patients with EGFR mutation, treated with first- or second-generation EGFR TKI therapy and developing resistance due to the mutation called T790M.

You are involved in the development of new drugs for lung cancer. Do many drugs fail early stage trials?
In the last 15 years, several attempts were made in order to introduce new treatments and new approaches in the lung cancer therapeutic algorithm. Several improvements have been done, but unfortunately there are many more failures already in Phase I and, even worse, in Phase III trials. In fact, it could happen that some positive signals are coming from a Phase II study, inducing pharma companies and researchers to move forward in the development.

What are the most promising new drugs in development for lung cancer?
In my opinion, mainly focusing on advanced NSCLC, there are at least three turning points in the last 15 years: the introduction of the concept of histology as a predictive factor due to the results of the pemetrexed registration trial in first line; the start of precision medicine in thoracic oncology with the identification of two druggable biomarkers (EGFR and Alk) and the new world of immunotherapy starting from the results of nivolumab in squamous carcinoma up to pembrolizumab data in the first line.

Do you believe there is a future role for targeted agents as adjuvant therapy for lung cancer?
Up to now we do not have positive results in this context and no background supporting the biomarker tests in early NSCLC completely resected, but this is still an open question and further (and more ‘modern’) trials are currently ongoing, like ALCHEMIST (A081105, E4512) or others (NCT02448797, NCT01405079).

You have been involved in a study analyzing genetic characteristics in young adults with lung cancer: is precision medicine a promising strategy to treat the disease in this age group?
Definitively yes: this subgroup of patients present with a completely different molecular profile compared with the adult counterpart showing, for instance, a different (and higher) expression of Alk and ROS1 rearrangements and a sex differentiation even more pronounced than what is already known in adult patients.

Crizotinib has proven effective in ALK-rearranged non-small-cell lung cancer, but patients often develop resistance. What strategies & therapies do we have to overcome this?
Several new Alk inhibitors are currently available mainly within clinical trials. Some of them (i.e., ceritinib, alectinib or brigatinib) have already been approved by regulatory agencies with a clear efficacy in Alk-positive pretreated patients and others demonstrated efficacy in Phase I/II trials.

Part of your research has focused on gender differences in lung cancer. Could you tell us about your work with Women Against Lung Cancer in Europe?
Women Against Lung Cancer in Europe (WALCE) was founded in 2006 to raise awareness with regard to the increase of incidence and mortality of lung cancer among women. Ten years later, WALCE is a European Advocacy Group doing information, prevention, support for all the patients with lung cancer and their families. WALCE is cooperating with other Advocacies across the world and with scientific Societies dealing with thoracic malignancies.

Where do you see your own research heading over the next 10 years?
I will continue with my commitment in primary prevention because smoking cessation is the real way to ensure that lung cancer could become a rare disease. Many results have been reached in the multidisciplinary approach but many others are still to be done. In the precision medicine, we are just at the beginning and many efforts need to be made to get more drugs for further targets. Immunotherapy is for sure a great innovation for thoracic malignancies but many sides remain obscure in this context.
and some years will be needed to resolve all the questions that today are unresolved.

Disclaimer

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