EGFR Resisters Clinician Spotlight: Paul Stockhammer, MD

This month we have the honor of featuring Paul Stockhammer, MD, PhD. As a third-year resident at Yale School of Medicine last year, Dr Stockhammer received the Distinguished Young Investigator Research Award at the 2022 EGFR Research Summit for his work entitles "Co-occurring Alterations in Multiple Tumor Suppressor Genes Associate with Outcomes in Patients with EGFR-mutant Lung Cancer." Dr Stockhammer is a research member of the Politi Lab at Yale where he focuses on EGFR-driven lung cancer and drug resistance, with emphasis on studying the relationship between EGFR and co-occurring tumor suppressor gene alterations. The future of EGFR lung cancer research is bright!

What motivated you to get involved with lung cancer research? How did you do it?
I studied medicine in Austria at the border to Eastern Europe where lung cancer rates are notoriously high. Therefore, during my time as a medical student, I became confronted with the reality of how deadly and complex this heterogeneous disease is. However, I was also fortunate to witness swift advances in lung cancer research from discovering novel therapeutic targets to tailoring personalized treatment strategies. But despite all the achievements, lung cancer remains the leading cause of cancer-related death. The interplay between rapidly advancing research, biological and medical complexity, but also the close personal relationships with patients motivated me to get involved in lung cancer research as a physician scientist.

What research have you done that would have the most impact on our members with the EGFR mutation?
As an MD/PhD student in Vienna I became interested in why tumors from most patients with oncogene-mutated lung cancers (like the EGFR mutation) inevitably progress on targeted therapies. Resistance to specific drugs like osimertinib is attributable to complex biological processes and to date, is incompletely understood. This interest led me to the Lab of Dr. Katerina Politi during my time as a medical resident at the Yale School of Medicine. My recent work in the Politi Lab characterized a patient subgroup with very aggressive EGFR-mutated lung cancer whose cancers had certain additional mutations in genes called tumor suppressor genes. Patients with these tumors responded less to standard-of-care EGFR inhibitors, they had more metastases, and they had shorter progression-free and overall survival. Therefore, our work underlines the importance of testing for co-mutations, and it suggests that those patients with tumors with co-occurring tumor suppressor gene mutations may be most in need of new treatment approaches beyond osimertinib.

What new projects are you working on?
Although we could recently demonstrate that EGFR-mutated lung cancers with certain co-mutations in tumor suppressor genes may behave more aggressively in the clinical context, the biological features of these aggressive lung cancers remain unclear. Building upon my recent work at Yale, I am planning to further investigate the biological

underpinnings of these specific lung cancers. We hypothesize that these specific tumors are not only associated with an aggressive disease course but also with unique targetable molecular features. This project could have significant implications for understanding the differential outcomes to EGFR-inhibitors like osimertinib, and it will support identifying patients for alternative or more aggressive therapies early in their disease course.

What was treating lung cancer/lung cancer research like when you first started to practice, and when was that?
Although I have only practiced as a physician for a few years, tremendous progress has been made over that time period. By identifying and characterizing more and more driver mutations like the EGFR mutations or mutations in HER2, our treatment landscape in lung cancer has drastically transformed. While chemotherapy was offered to most patients with lung cancer in the past, current treatment algorithms incorporate a wide variety of different agents tailored to each specific patient and their specific cancer.

What do you think lung cancer treatment will look like five years from now? Lung cancer treatment will be more and more personalized and tailored to the individual patient and their specific cancer. In EGFR-mutated lung cancer, future studies will hopefully help us to select the best treatment for each patient, whether this is in the adjuvant setting after surgery or whether this is at a more advanced disease stage. I think that these future decisions will be influenced by many factors including type of EGFR mutation, co-mutations in other genes, liquid biopsy results before and during treatment, and which parts of the body are involved by the cancer.

What treatments/research of interest do you consider will make a significant impact in the not-too-distant future?
Investigations into drug resistance to targeted therapies and understanding its biological mechanisms will be essential. A better understanding of these aspects will help us to provide personalized treatments that can result in long-lasting and sustained treatment responses in patients with EGFR-mutant lung cancer. We also must learn to better understand which patients may need combination treatments beyond osimertinib monotherapy as their first-line treatment strategy and for which patients osimertinib alone is sufficient.

How could treatment be done differently at this time to improve care? One big challenge is to universally provide access to medications like osimertinib and to make these medications more affordable for the community affected by lung cancer. Social determinants of health and inequity are major factors that sadly continue to influence equitable access to our latest medical innovations. In addition, recent studies highlight the importance of obtaining tumor genomic profiling either from blood or tissue before and during treatment to guide treatment decisions in patients with lung cancer.

Do you have any advice for people considering clinical trials? Patient advocacy groups

like the EGFR Resisters and the KRAS Kickers are wonderful opportunities for patients and their families to stay up-to-date on the most recent
science in the field and to learn about potential clinical trial opportunities. At scientific meetings over the past year, I have met some amazing members of those advocacy groups – their endless efforts to raise awareness and bring science and research closer to patients impacted by lung cancer is so important. Clinical trials are great opportunities to receive novel drugs and particularly patients with EGFR-mutated lung cancer with rare features (i.e. rare EGFR mutations) could substantially benefit from getting enrolled in these trials.

Is there anything else you would like our readers to know?
Although tremendous progress has been made in treating EGFR-mutated lung cancer, there still exist many unmet needs. As example, most patients are still diagnosed at an advanced stage when the cancer has already spread to other body parts. In this context, it will be crucial to continue efforts to develop and bring innovative methods for early detection and innovative treatments to all patients affected by lung cancer regardless of their socio-economic determinants.