

Dr. Howard West: lung cancer research, a field of great optimism

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Expert's introduction

Dr. Howard West, medical oncologist and medical director Thoracic Oncology Program at the Swedish Cancer Institute in Seattle, Washington, USA. He is also the founder and President of a global non-profit for cancer education for patients called Global Research for Advancing Cancer Education (GRACE) at cancergrace.org (Figure 1).

Interview questions

ATM: *As a distinguished invited speaker for the WCLC 2017, you had an excellent presentation, which was well received by the audience. Would you like to summarize some main points to share with us?*

Dr. West: I was the presenter for three abstracts about acquired resistance in EGFR mutation-positive advanced non-small cell lung cancer (NSCLC), and I think the key point to this was that the target MET is likely to become increasingly recognized and clinically relevant. There are several MET inhibitors out there, and one of them was the subject of one of the abstracts, a drug called savolitinib, in combination with gefitinib, for patients with acquired resistance to an initial EGFR inhibitor. This drug combination of gefitinib ongoing with savolitinib was associated with a very good efficacy overall, especially in the subset of patients who were negative for the acquired resistance T79M mutation. We look forward to more work on this being done.

At the same time, there is other work being done looking at other mechanisms of acquired resistance, as well as looking at MET and how well that associates with activity with EGFR inhibitors. What I would say is that there is still a lot unknown about how best to test for MET and what we should consider to be truly positive disease. We need to work more on clarifying what should constitute “MET-positive” in testing, since part of the variability in results may be related to very different thresholds of



Figure 1 Dr. Howard West with AME groups.

how investigators defined “MET-positive” in one trial vs. another.

I would also say that a key point of my presentation was that we need to ensure that the frequency of the targets and the efficacy of the drugs for them are great enough to make it worth general oncologists out there in the world to do this testing, and that it's not just something of interest for only the most focused on lung cancer. It has to be of a big enough impact to change the world of treatment.

ATM: *Some people may say, there will be a day when molecular markers finally replace first line treatment option for advanced NSCLC. What is your opinion on it?*

Dr. West: I think we are always continuing to move toward more precision medicine. We are looking at a more limited role for general cancer drugs like chemotherapy, and more toward targeted therapies for patients. However, in different parts of the world, there are different patterns of lung cancer. In Asia, there are far more patients with driver mutations, and I would say that it makes sense to think more and more about lung cancer as being based on one specific driver or another. In many parts of the US, in Europe and some other parts of the world, most lung cancers are still

caused primarily by smoking, and often smoking for a long time, and instead of there being one driver mutation, there's likely to be a much broader array of markers that contribute in a smaller way, rather than one main driver mutation. So, I don't think we are going to move away from chemotherapy and only be looking at lung cancer as driver mutation-based, because I think that that really only applies to a subset of people. Chemotherapy, which is still a broad utility, and immunotherapy—which is probably particularly helpful for a subset for people but still potentially, if not likely, broadly useful for many people—is going to still have a big role. I don't think we are moving away from general treatments and only towards very specific precision medicine, but the role for it is going to grow over time.

ATM: As an outstanding expert in the field, would you like to share your opinions/suggestions with Chinese experts on future studies on diagnosis and treatment of NSCLC?

Dr. West: I think that the field of lung cancer is moving toward identifying more and more driver mutations, so some of the biggest changes that we are likely to see are that next-generation sequencing (NGS) is likely to become a standard treatment approach, replacing individual testing of two, three, or four markers, and instead we are likely to move toward testing everybody with an NGS panel that can look for dozens, or even more than a hundred different genes right at the time of diagnosis. At that initial diagnosis, we're also going to be looking at immune biomarkers, whether that be PD-L1, tumor mutational burden, or others. I think we're also going to be doing far more liquid biopsies in the future, not necessarily to replace initial tissue biopsies at the time of diagnosis, but to monitor disease at a different level and with more frequency. That is going to overcome some of the risks and inconvenience of doing multiple tissue biopsies over time and as a patient develops resistance to treatment. I believe that the biggest diagnostic and overall therapeutic changes besides the growing use of targeted therapies including retesting for acquired resistance and immunotherapy being broadly used, will be NGS testing really becoming a standard upfront, and more and more of liquid biopsies being used, particularly because they are so easy to incorporate serially over the course of time and treatment for patients.

ATM: Along the way to be an excellent researcher, would you like to share with us any stories about it? What encourage you to choose the career/field?

Dr. West: I've been focused on lung cancer for about 18 to 20 years. For much of the beginning of that time, for the first 5 to 10 years, many people—many of my colleagues and others—would ask “why did you go into lung cancer?” because it seemed like such a bleak area of oncology. There were few advances, patients didn't do very well, and it just seemed like it was a dead end. Now, it's interesting that over the last 10 years, lung cancer has become, in many ways, the envy of other areas of oncology. There are many areas that have had great improvements, but lung cancer is now an area of incredible optimism, and it's remarkable for me to think back on a time where it seemed like there were so few options and it was so hard to improve on the old standards. That's because now the biggest challenges we have are related to keeping up with all of the advances; the standards change all the time, the new targets, the role of immunotherapy, the incredible growth of so many new treatment options.

These developments have made it such a richer field, and what's really important is the optimism about it. So, for most of the first 5–10 years I was in the field, we were resigned to expecting patients to live usually just a few months longer for treatment, and not many of our patients living beyond the year. Now, fast forward 10 to 15 years, and a growing fraction of our patients, a pretty significant number, are now living years, not just 1 or 2 years, but potentially 3 and 4 and 5 or more years. And that happens when we find an EGFR mutation, or an ALK rearrangement, or a ROS1, or now many of our patients on immunotherapy are living for years and years. So, I think that for some patients, it's a huge win, and for everybody, it gives incredibly more hope than we had before, not just that they would have one of these targets and benefit from it, but we can also see how much we're gaining.

It's hard to keep up, but that's a wonderful problem to have, and it just makes us feel that these marks of improvement suggest that we're going to continue to do more and more and help our patients live for longer into the future. I would say that it's been remarkable: the turnaround of lung cancer from being a very difficult area to study to being a very robust and rich area with lots of new developments all the time that are still ongoing.



Figure 2 Interview with Dr. Howard West: lung cancer research, a field of great optimism (1).

Available online: <http://asvidett.amegroups.com/article/view/22692>

For more detail of the interview, please refer to the following video (*Figure 2*).

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Footnote

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1. Ling N, Poon B. Interview with Dr. Howard West: lung cancer research, a field of great optimism. *Asvide* 2018;5:059. <http://asvidett.amegroups.com/article/view/22692>

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