The Role of Targeted Therapy Post-Resection

TRANSCRIPT & FIGURES
Since the mid-2000s we've known that many patients who have non-small cell lung cancer, particularly the adenocarcinoma type, have particular gene mutations that we can identify and when we find them, treat with specific new drugs. We know this data from patients with metastatic lung cancer – the first to be discovered was EGFR or epidermal growth factor receptor, then ALK or anaplastic lymphoma kinase. Now there’s a very long list of gene mutations that we can identify when we look in patients with advanced stage lung cancer, and when we find them, offer specific targeted therapy that can have a very high likelihood of shrinking the tumor. This has really changed the way we think about and treat advanced stage lung cancer. However we haven’t figured out how to best use those treatments for patients who have earlier stages of lung cancer.

So in the setting of an early stage lung cancer that’s been removed with surgery, patients are theoretically cured at that point. Chemotherapy has been proven to lower the chance of the cancer coming back, but when you find one of these mutations in the tumor, the temptation is to give one of these targeted drugs. That strategy has been looked at in multiple clinical trials and we still don’t have a straightforward answer.

The largest trial to look at this so far was called the RADIANT trial and in that trial, after getting chemotherapy if that was the right thing for them, patients either received the EGFR drug called erlotinib, or a placebo. Now most of those patients in that trial actually did not have a specific mutation in EGFR because the study was designed before we knew about how important those mutations were. In the subset of patients who did have the EGFR mutation, those getting erlotinib seemed to have more time before the
cancer came back, but if you looked at their overall survival, it wasn’t any different than the patients who had been on the placebo arm. The theory is that those who were on the placebo arm who had the cancer come back, when it came back they were then able to get erlotinib or a similar drug and have the same benefit. So it’s not clear that starting the erlotinib right at the time of surgery actually helps people live longer, though it might slow down the time to recurrence.

That’s obviously not a complete answer so there are more studies happening now trying to get a better sense of what we should do in that setting. There are a couple of trials in China, actually several trials in China, a study in Japan, and now a big study in the United States, all with the same general idea that a patient who has a tumor resected or removed by surgery, who is shown to have an EGFR mutation in that tumor, is randomized to either get an EGFR drug or to get placebo. Some of the studies have chemotherapy before or after, some compare it to chemotherapy, so there are some differences, but the general idea is whether or not giving the EGFR targeted drug will actually help people be cured or live longer versus waiting, and then for those who do have recurrence, giving it at that time. So those are really important trials that are ongoing and we’ll hope to know the answers in the next few years.

For the patients with the ALK translocation in the United States, the big trial called ALCHEMIST is open not just to EGFR but also to ALK patients. What that trial is about is asking that any patient who has a surgery at a site that’s participating in ALCHEMIST have part of their tissue from the tumor sent in to a central laboratory to be tested for EGFR or ALK. Those patients who
have EGFR are then randomized to either get the EGFR drug erlotinib, or to get a placebo pill, and those who have ALK to get the ALK drug crizotinib versus a placebo pill. Over time people will be followed to see – does this change when the cancer comes back, and does it ultimately change overall survival for the patients where the cancer does come back?

So this is a really critical trial and it’s going to help us know what the best way is to use these targeted drugs for patients in this setting. Until we have those trial results back, I do not recommend that patients get the EGFR or ALK targeted drugs after surgery because we just don’t know if that’s going to help them live longer.
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