Patterns of Acquired Resistance to EGFR TKIs in EGFR Mutation-Positive NSCLC

TRANSCRIPT & FIGURES
For patients with EGFR mutant lung cancer, we generally recommend initial therapy with an EGFR tyrosine-kinase inhibitor – so, that’s gefitinib, erlotinib, or afatinib. We generally see significant tumor shrinkage with these drugs, but after time, patients eventually develop resistance to these therapies. The time until resistance really can vary dramatically, from three months, to even a few years down the road, but eventually patients do develop resistance.

How that resistance manifests is really important for deciding how to deal with the consequences of resistance. So, if we see resistance develop in a handful of sites and it’s very slow growth, we may actually just monitor that disease progression, acknowledging that the disease is beginning to become resistant, but recognizing that we don’t want to make changes in therapy too quickly. Importantly, if there is a single site of resistance, and if it’s a site that may cause symptoms or a site that is causing symptoms, such as a painful boney metastasis, it’s a very reasonable approach to target just that site that’s developing resistance, so that we can continue controlling the rest of the body with the oral medication, and then control the single-site progression – for instance, if a lung nodule has popped up that wasn’t there before, and is growing, it would be reasonable to consider radiation therapy for that lung nodule, or even, in some cases, surgical resection of that lung nodule to remove that resistant nodule, and observe how patients do afterward.

In a retrospective series from my institution, we took a handful of patients who had been treated this way – where, after a single site of resistance developed, we did radiation or surgery, for that site of resistance, and we found that the time until we had to make a change in their systemic therapy,
i.e., drop the EGFR tyrosine-kinase inhibitor, or add chemotherapy, was over a year for most patients. And so, as a consequence, I think we spared a change in therapy for a year, and we generally helped patients.

Now, of course, this needs to be studied more, but I think this is a reasonable strategy for patients with single-site resistance.
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