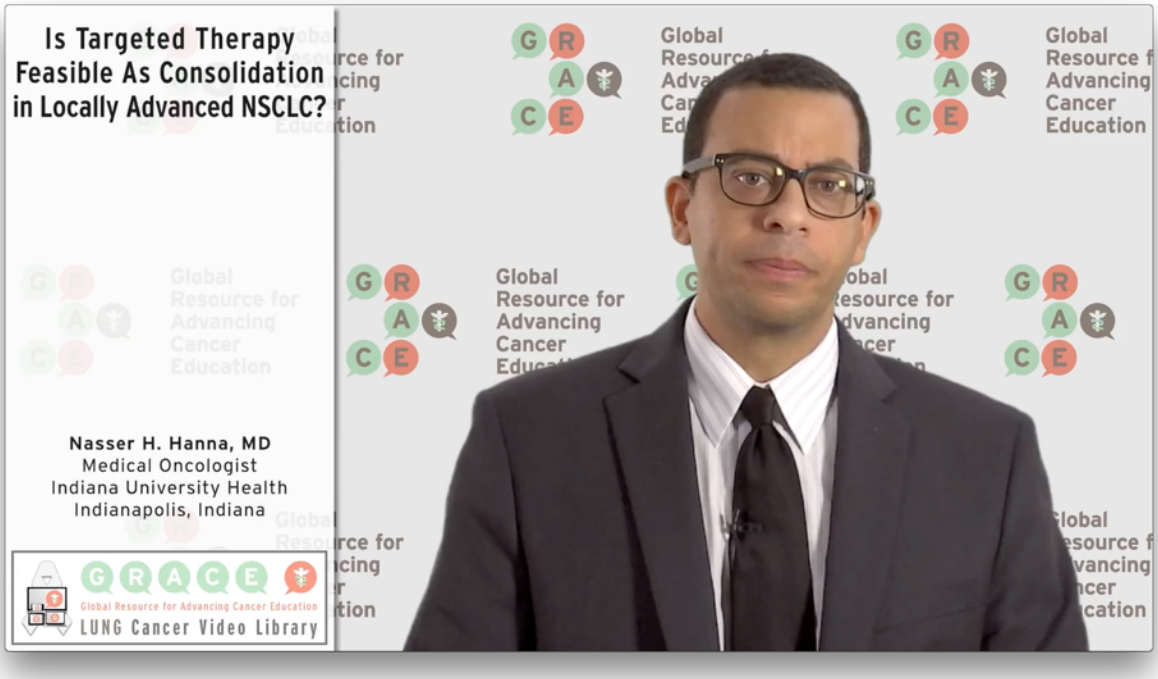
Global Resource for Advancing Cancer Education

LUNG Cancer Video Library

Is Targeted Therapy Feasible As Consolidation in Locally Advanced NSCLC?



TRANSCRIPT & FIGURES

Because those strategies testing additional systemic therapy utilized chemotherapy and those strategies did not improve outcomes compared to concurrent chemoradiation alone, we looked to try to give other forms of systemic therapy that were not chemotherapy to see if perhaps that would improve outcomes. Beginning in the 2000s there were a number of new drugs that appeared to be active in people with lung cancer and these are what we call molecularly targeted therapies. The first of these molecularly targeted therapies targeted a certain growth receptor on the surface of cancer cells, and this is called the epidermal growth factor receptor (EGFR) and we had a drug at the time which would target cancer cells that expressed this epidermal growth factor receptor. Well we understood in the 2000s that the vast majority of people with lung cancer have tumors that overexpress these growth receptors on the surface.

So clinical trials were designed to incorporate these new molecularly targeted therapies into the backbone of therapy that we had already established. Probably the best known of these trials was conducted by one of the United States cooperative groups in which all patients with stage III unresectable non-small cell lung cancer received the standard concurrent chemotherapy and radiation therapy backbone. Now in this trial patients were allowed to receive additional chemotherapy after that but the bottom line with this trial and the importance of this trial is then at that point patients were then randomized to receive either this molecularly targeted therapy or to receive a placebo.

At the time, again, this was the most effective molecularly targeted therapy we had in lung cancer and this was our greatest hope for further

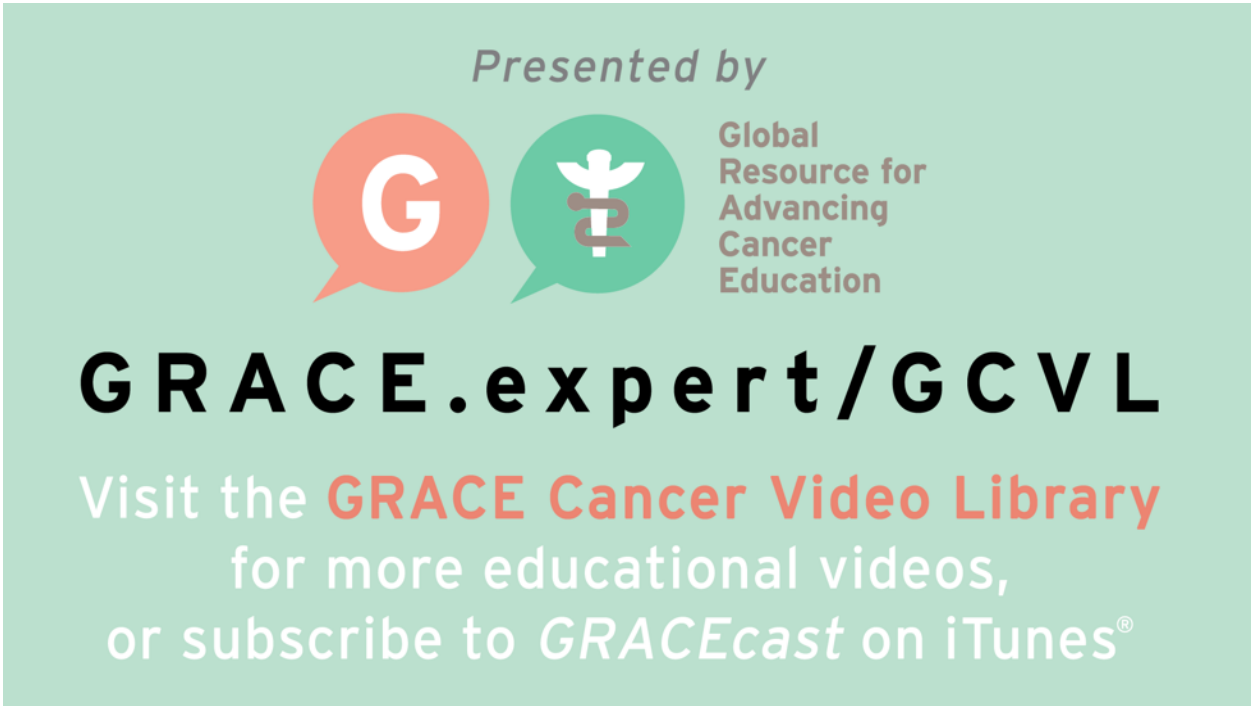
advancement over just giving concurrent chemoradiation alone. This drug was called gefitinib, it is approved by the FDA today and it is commercially available for people who have metastatic disease. What this trial demonstrated was giving that drug after chemotherapy and radiation therapy did not improve outcomes. In fact more people who received placebo had long term survival compared to those who received the gefitinib. So that hypothesis was utterly rejected and clearly is not the way forward.

Since that trial was designed we've come to better understand which patients actually benefit from these drugs that target the epidermal growth factor receptor. In fact we have new targets including a gene called anaplastic lymphoma kinase or the ALK gene and we have molecularly targeted therapy against tumors that have that gene abnormality.

So the current state of the art clinical trials testing molecularly targeted therapy are not just indiscriminately giving everybody the drugs, but they're testing the idea that perhaps there are subsets of patients who would preferentially benefit from these targeted therapies. So one of the United States cooperative groups right now is conducting a clinical trial for patients with stage III unresectable disease. Everyone is getting concurrent chemoradiation, but those patients who have either an abnormality in the epidermal growth factor receptor gene, or in the anaplastic lymphoma kinase gene are also being randomized to receive the molecularly targeted therapy or not.

So this is a very different idea, this is not just empirically giving everybody these molecularly targeted therapies, but it's targeting patients for these

drugs based on the molecular biology of their disease. Now these trials are ongoing right now and I think we're optimistic and we're hopeful because we've seen the activity of these targeted drugs in patients who have metastatic disease. Perhaps we'll see some improvements in outcomes in these targeted populations — that question is probably not really going to have an answer for about two or three years. That's the current state of the art treatment that's being tested regarding molecularly targeted therapy in stage III cancer.



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