Induction Chemotherapy Followed by Chemo/Radiation for Stage III NSCLC
One of the areas of controversy is with regard to induction chemotherapy, followed by chemoradiotherapy in stage III disease. I mentioned before that systemic micrometastatic disease is a huge problem in these patients, and one has to give adequate, effective chemotherapy in this setting. We typically give chemotherapy with radiation, but radiotherapy strategies typically last six to seven weeks, and therefore, that would really account for essentially two cycles of chemotherapy. Now, in stage II or III when we are giving adjuvant therapy, or in the metastatic stage IV setting, our current standard is to give four cycles of chemotherapy in that setting, maybe sometimes six in the stage IV setting, so I've always wondered why would we just give two cycles concurrent with chemoradiotherapy in the stage III setting?

However, I will tell you that all the level one evidence does not routinely support the use of more chemotherapy, other than during the radiotherapy. Obviously, it could be given before, as so-called induction, or it could be given after chemoradiation, so-called consolidation therapy. Many investigators have pursued giving two cycles prior to initiation of chemoradiation – that's a strategy that I like personally, and frequently do in my practice. I don't have level one evidence to suggest that it's a strategy that has, in clinical trials, which in my opinion have been limited and relatively small in number, so relatively underpowered in this setting – but the advantage of induction therapy is, often patients are symptomatic, the response rates tend to be in the 40-60%, depending upon which study you look at – a response makes the patient feel better because their symptoms may get better, but the other thing it does is that it may allow a smaller field of radiation, if you believe that it's okay to treat the volume of cancer that is present after
chemotherapy, which is what we do at our particular center. So it may allow a smaller field of radiation be using induction therapy, that may then reduce the toxicities you may see during chemoradiation.

Again, this strategy has not been proven at the phase III level one evidence. However, it’s very commonly used and I will also note that it’s very common for a practicing oncologist to recommend two cycles of consolidation chemotherapy if the initial treatment is concurrent chemoradiotherapy. So rather than give chemotherapy before, it’s given afterwards. Again, not a proven strategy at the phase III level one evidence point of view, however, many of our major clinical trials done in cooperative groups allow two cycles as consolidation therapy, which is typically what is commonly done in practice.

My personal bias is that you should think about giving four cycles in this particular setting. I think two cycles are inadequate to control micrometastatic disease, particularly if during radiation, the chemotherapy strategy that is pursued is low-dose weekly approaches, which may not be the optimal way to control systemic disease.
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