

Serum Tumor Markers in Lung Cancer Management

I've been meaning to write on tumor markers detectable in the blood for the management of lung cancer. These are proteins that are produced by some tumors, and the idea is that the levels of the tumor markers in the blood can potentially be used to monitor the status of the disease. For prostate-specific antigen in prostate cancer, [carcinoembryonic antigen](#) in colon cancer, CA19-9 in pancreatic cancer, and several others in breast or ovarian cancer, these markers have been well studied and are commonly used. The more commonly used tumor markers in lung cancer are CEA, and sometimes CA-125, as well as occasionally some others.

The problem is that there's so little written and even carefully researched on these issues in lung cancer. In one [very good clinical textbook on lung cancer](#), tumor markers are mentioned on just a couple of the >450 pages. The [National Comprehensive Cancer Network \(NCCN\)](#) guidelines for NSCLC and SCLC do not have any mention of tumor markers, and they really have no standard role in management or treatment, which is why the use of them is so variable in the real world. Many experts do not consider there to be any real role for tumor markers in lung cancer. There are some very highly regarded cancer centers that as a policy **never** check or use tumor markers in managing lung cancer.

There are several important limitations in the use of serum tumor markers. Several of the proteins seen on lung cancers are the same ones seen on other cancers, and CEA is also elevated in smokers without cancer, so they aren't specific to lung cancer. Also, if a marker is going to be very helpful, it should be expressed on the vast majority of the cancers you're following, but different cancers express different proteins or none at all ([abstract here](#)). However, there are so many proteins being studied by just a handful of groups in the world that there has never been a critical mass of consensus leading to any standards here. It's basically individual preference and style of the oncologist that leads to whether tumor markers are checked and followed.

There are a few basic principles about tumor markers. Some studies have shown individual markers at the time of diagnosis to be predictive of better or worse long-term outcome in NSCLC ([abstract here](#)) or SCLC ([abstract here](#)). Here is a figure that goes back more than 20 years, from an article on the prognostic value of CEA in SCLC:



We can say a few principles about tumor markers. There's some limited evidence that certain ones can be predictive of worse outcomes if they're elevated at diagnosis, but there is no routine recommendation for checking this. Some people are interested in using factors like elevated markers to help refine recommendations about which early stage patients should receive post-operative chemo or not, but similar work is being done on tumor [gene signatures](#),

proteins like [ERCC1 expression on resected tumors](#), and other techniques. There is also some limited evidence that a rising CEA after surgery can predict a recurrence before imaging picks it up ([abstract here](#)). So perhaps finding a rising CEA would lead me to do a scan earlier rather than later to document a recurrence, but the tough question is how that would really help. There are a few cases in which a recurrence is detected when its localized and still potentially treatable with curative intent, but unfortunately the clear majority of cases have recurrences distantly. So the earlier detection allows people to learn they have advanced disease more readily, but it doesn't clearly improve treatment options or outcomes compared to finding out when you otherwise would without the head start of the blood test.

The other key question is on using serum tumor markers to follow response, such as in patients with more advanced disease. This is really not well studied at all, but there is some work that suggests that response of various tumor markers after four weeks on treatment such as Iressa is well correlated with subsequent imaging-based responses, as well as survival ([abstract here](#)). Other work has shown in a variety of tumors treated with a range of treatments that there is a good but not perfect correlation of tumor marker trends with response ([abstract here](#)). My take on the situation is similar to my view on use of PET scan results and standard uptake values (SUVs) in assessing response and making treatment decisions in lung cancer. CT scans are a much better studied standard, and I would personally be very reluctant to stop a treatment that is not associated with progression on CT just because a tumor marker or SUV is rising. If you have to try so hard to find progression that it doesn't appear on a CT, which shows a lot of detail, I would be disinclined to abandon that treatment. We don't have enough effective therapies in lung cancer that I would want to toss a treatment that is pretty much associated with stable disease too quickly. But I do think that they can give some useful early feedback that can give a sense of when the next scans should be done. I hope more research helps us integrate tumor markers intelligently into the practice of lung cancer, because I do think they could prove to be helpful once we clarify their role.

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