Time to Response to Immunotherapy and the Concept of Pseudoprogression

TRANSCRIPT & FIGURES
So, we have seen, certainly, some variability in the time to response; we have seen some people who will even have palpable lesions that will shrink, you know, within days – although that is rare. In general, what we find is that, generally, somewhere around 6 to 8 weeks is when we see patients who are having response to drug. It tends to be quite rapid – when you look at the clinical data, you can see that probably most of the patients who have what we call a clinical response to these drugs, that response occurs probably at the first imaging analysis, usually somewhere about two months after starting. Although there has always been this sense that it will take a long period of time for someone to respond to an immune therapy, and that is true, for instance, compared to a standard chemotherapy, where the effects are often seen within a couple of weeks, here it tends to be delayed from that, but it doesn't tend to be delayed for months and months.

One other important issue to address is this issue of pseudoprogression, and this is something that people in the immunotherapy field have talked about for a long time, that if you have an effective immunotherapy, that you may have immune cells that infiltrate into the tumor and, as a result, rather than getting smaller, that the tumor would actually get larger. That could certainly happen over a short period of time, but what I would say, to date, is it’s not something we've seen a lot in lung cancer. Our colleagues in melanoma certainly report this as being a significant issue – patients who will have initial growth of their tumor on imaging, and then, afterwards, will have shrinking. We certainly do have several intriguing anecdotes, sort of individual patients that people will describe who have had, sort of, increases in their tumor volume, but then get better, but I would say that it is actually quite uncommon in lung cancer.
What we do see with some frequency is someone who will develop a new lesion. So, for instance, maybe they’ll have three areas that you’re following, all of them will get a little bit better, but then you will find one area that is a new area, that’s, you know, a centimeter and a half, that shows up on scans. By our typical way of evaluating radiographs, we would consider that to be progression. In my clinic, and as part of clinical trials, we’ve incorporated sort of different evaluations, that have, in some cases, allowed patents in that setting to continue on therapy. And, what I would say is, in somebody who is feeling good, who has an ambiguous response, one like what I mentioned, where several areas got better, but one area is new, or one area grew while other areas got better, but is clinically doing well – it may be worth continuing that patient on drug. But, when I see patients in second opinion and things like that, I will say that I much more frequently tell them that it is time to stop the immune checkpoint inhibitor, than to continue and hope for pseudoprogression. That, I would say, is very rare to see; we treated 98 patients at UCLA on the KEYNOTE-001 study, and I can’t think of a single patient that had, what we would call, sort of a flare response, where everything on the scan got worse, and then subsequently got better. So, I can’t give you an exact percentage, but what I would say is that it is rare. The thing that’s going to be more important is trying to interpret some of these ambiguous radiographic responses, which can be seen, but if everything is getting worse on the scan, what I’ve told people is, almost certainly, it means that the drug is not working.
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