

# cancer NEWSLINE

>> Welcome to Cancer News Line; your source for news on cancer research, diagnosis, treatment, and prevention. I'm your host Dr. Oliver Bogler. Our guest is Dr. David Hong, professor in the Department of Investigational Cancer Therapeutics and we'll be talking about targeted therapy versus immunotherapy. Dr. Hong there's a lot of excitement about targeted therapy precision medicine and also immunotherapy. Can you define these two for us and tell us a little bit about how they work?

>> Targeted therapy, one can argue, is therapy that is specifically targeted to either mutations, amplifications, or other kinds of molecular aberrations that are often times found in cancer. The classic example of this is imatinib, which was the first really drug that was identified to target BCR ABL in chronic myelogenous leukemia, but since then, there's been, just as there has been immunotherapy, an explosion of drugs identifying targets within cancers that specifically have benefited many cancer patients since, you know the development of this idea of target therapy. Immunotherapy, in contrast, but one can argue in some overlap, is different in the sense that its primary objective is to kind of activate the immune system to target cancer. I think there have been many pioneers that have taken many years to eventually bring to fruition immunotherapy, including Jim Allison here at MD Anderson, and the most recent immunotherapies have really worked to activate cytotoxic T cells and other innate immune cells to target cancer cells. Or, certain T cells, in patients, have been reengineered and given back to patients, such as these new CAR T cells that have been recently approved in ALL and also lymphoma.

>> So, it sounds like some of the immunotherapies are also targeted directly to the patient.

>> Yeah, and the reason I say there's an overlap is that I think there's been increasing evidence that certain subsets of patients, for example, let's call microsatellite instability high patients, which you can either identify by genomic analysis or routine immunohistochemistry, has shown that is definitely, that immunotherapy like Atezolizumab or Nivolumab has activity in these patients because these patients with high mutational burden, such as patients with, it's called high mutational load, tend to have, express what are called neoantigens on the tumor which allow for these, these activated cytotoxic T cells to actually that attack and kill cancer.

>> So, from the patient's perspective, how do you choose? If you're considering entering a clinical trial and you have multiple options and some of them are targeted and some of them are immunotherapy, how do you choose?

>> That's a really good question. I think, it depends on what stage of the trial. Most, obviously there's a difference between phase one, two, three trials. Most phase two and three trials are specifically targeted to either a specific tumor types or specific targeted populations. And so, in that context, usually phase two and phase three trials have already demonstrated probably some evidence of activity, whether it's immunotherapy or target therapy, in the phase one setting. Right? So, so in that context,

that, you know if your doctor or a doctor here at MD Anderson is offering you a phase two clinical trial, it's probably because there's been some activity, whether it's targeted or immunotherapy, based upon early phase one and phase one expansion data. So, in the end, I think, you know you want to get onto a trial that is going to hopefully work, right? Or has some level of activity and that's, so I don't necessarily know if I was a patient, you know would say I have to have immunotherapy or I have to have targeted therapy. You probably want to get onto a trial that may have some level of activity and usually in a phase two or phase three trial, there's probably some evidence that there's some activity in that context.

>> And I guess it depends a lot on just specific nature of your tumor, what kind of mutations you carry, as you said earlier, so.

>> Correct. Correct, and you know increasingly more, at least here at MD Anderson, we're profiling patients early on and patients are often times being, you know their tumors are being profiled by, what's called next gene sequencing, in the community with vendors such as Foundation Medicine or Caris Diagnostics. So, we see that often and there are what are called, can often be what are called actionable mutations or actionable molecular alterations. Actionable in the context of 1) there is a mutation or aberration we think is driving that cancer and 2), that there's actually a drug or a trial that may actually be able to target that aberration.

>> So, if you have such an actionable mutation, then the precision medicine or targeted therapy is probably the best choice, at least initially.

>> That may be a very good choice for you, if you actually have an actionable mutation. Yes.

>> Do you see a future where these two areas will combine where immunotherapy --

>> Yeah, I definitely think that's what's kind of next reiteration of all of this and many of the ongoing combination trials, both in the phase one setting, phase two setting, are looking to see whether patients with certain targetable actionable mutations may benefit with the addition of not only just immunotherapy, but even immunotherapy plus chemotherapy, etcetera. So, that definitely is kind of where all of this is leading. I think everybody believes that immunotherapy, in some settings, is definitely beneficial, but really, it's in the combination of, rationally designed combination trials that will ultimately, we will have greater benefit.

>> Thank you very much Dr. Hong for sharing your knowledge with our listeners.

>> Thank you for inviting me.

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