Advances in Immunotherapy in Head and Neck Cancer

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TRANSCRIPT

(JW) Hello, I'm Jared Weiss, Vice President of Cancer GRACE and a Medical Oncologist at the University of North Carolina Chapel Hill and I'm here with my colleague. (JB) I'm Josh Bauml, I am a Medical Oncologist at the University of Pennsylvania.

(JW) I think everyone's been waiting for the results of some major immunotherapy studies where immunotherapy alone or in combination with chemotherapy is supposed to replace our standard of care old-school chemotherapy regimens, did we get that? (JB) We did not. You know, ASCO had a lot of data about combing things with immunotherapy. There were a lot of positive trails in lung cancer, but we didn't get very many big trails of those combinations in head and neck cancer with results or with positive results. What we did hear about is the fact that when we give immunotherapy, patients quality of life is maintained so we got data from keynote 40 which randomized patients to Pembrolizumab or an investigators choice of regular chemotherapy (Docetaxel/Methotrexate) mostly getting Docetaxel. Pretty rough stuff. What we found is exactly what we would expect which is patient's quality of life is better when they're receiving Pembrolizumab. (JW) But, I think that's a big deal. It's not surprising, but I think confirming it matters. (JB) I absolutely think it's important. (JW) That's why most of us come to the office. It's why most of our patients come to see us in the office, to make people feel better.

(JB) That's right, but one of the thing we do have to remember is that when we give immunotherapy sometimes there are what we call immune mediated adverse event. We're amplifying the immune system to kill the cancer, to fight the cancer, and so what I warn my patients of is "Look, your immune system could go crazy. It could attack any part of your body. It could attack your heart, your lungs, your kidneys, your liver, your skin, anything."

(JB) One of the questions that patients often ask is “If that happens, is my cancer still going to be responding to the treatment? What’s going to happen?” And I think that’s an important question, have we heard anything about that? (JW) We did. So, I counseled my patients very similar maybe not quite those words, I suspect you might not use quite those words either, but maybe. (JB) No, I use those words. I say, “It can go crazy.” It can attack any part of the body. (JW) So, I find some people get a little scared. I couch it in that most of these are really rare. But, I think the key point is we can’t say “Watch out for nausea and take this pill.” We can’t give them an “If ‘A’ then ‘B’” because it’s a long list of rarish things. We do have some examples before of toxicity being a surrogate for benefit. Bevacizumab in lung cancer may be rash with EGFR inhibitors in colorectal cancer and we saw hints of the same here. Where patients with immune related adverse events, most commonly rash and throwing off the thyroid had pretty meaningful improvements and outcomes. It was a roughly a tripling of response rate, roughly a tripling of progression-free survival, and a very meaningful improvement in survival.

(JB) One of the other things that is happening with immunotherapy which I think is very interesting is historically chemotherapy sort of second-line later line chemotherapy in head and neck cancer had not been very effective, but I thought there was a really neat abstract which looked at patients who received chemotherapy after failure of immunotherapy. They found the response rates were 20-30%, so quadruple what we would expect in this population and that I think is really important and exciting. What it implies is that the immunotherapy is working well beyond when we stop administering it. I think that’s exciting. It’s also important to remember that from a toxicity standpoint though, because it means that those side effects can happen long after the drug treatment is stopped.

(JW) So, immunotherapy is this big advance. I think all of us are rightfully excited about it. I think it also leaves a lot to be desired. It’s not curing, or at least not curing many people that these durable controls we want aren’t happening in a large enough proportion of patients. It’s easy to brush under the rug, but the truth is our average patient doesn’t respond to it. So, of course we do what investigators do. We study everything we can think of to try to make it better. We saw some data on those. Anything that excited you? (JB) So, I think one of the ones that a lot of my patients think about and a lot of doctors that I speak to think about is adding radiation to the immunotherapy. The logic here is that when you are using immunotherapy you have to identify what are called antigens; that is what the immune system identifies to kill. So, when you radiate something all the cells rupture and when those cells rupture they release a lot of antigens. (JW) Junk for the immune system to see and get pissed at. (JB) Exactly. So, basically the idea is if you radiate something that can create a vaccine which makes the immune system even more amped up to fight the cancer. There are some very exciting anecdotes, where people are on immunotherapy, they got one thing radiated, everything melted away; this is called the abscopal effect. Everyone’s trying to find the abscopal effect.

(JB) We saw two trials at ASCO this year, one in head and neck cancer and one in lung cancer. What they did was they gave patients radiation with immunotherapy. They randomized into either immunotherapy alone with the PD-1 inhibitor and the gave them… (JW) The same kind of radiation like we do for cure? (JB) It's a stereotactic radiation, a focal radiation, relatively well tolerated. (JW) So, big doses to a small area. (JW) Big doses to a small area with very few side effects and they tried to see if they could amp up the response. In head and neck cancer, we did not see an improvement in the outcomes really in any way. In lung cancer, there was a numeric increase in the response rate, but it did not reach statistical significance. These are small studies. To me what this means is radiation in and of itself is not going to make everyone respond to immunotherapy. There's not an easy solution for everyone. There might be some patients who benefit from that, who would benefit from that degree of adjuvant, but it's clearly not for everyone. I certainly wouldn't recommend that patients who want their immunotherapy to work better say "Oh, radiate something just to amp it up." That is clearly not a ready-to-go strategy.

(JW) What about on oncolytic vaccines, oncolytic viruses, excuse me? (JB) So, oncolytic viruses there was a study using T-Vec, a whole long name very difficult to say. (JW) I can't say it. I was almost an investigator on their Phase 3 and I can't say it. (JB) We are just going to say T-Vec. So, what did they find in that study? (JW) This idea was really appealing, and it was a lot of the same logic as what you expressed before which is that they were going to inject, so they have a virus and the virus is engineered to eat cancer cells. Viruses in general as you know infect a healthy cell, make lots of copies of themselves in the healthy cell, and burst the cell. So, the idea was that this would not only eat cancer but would be self-replicating; lots of antigen exposure in the way you just described, synergized well with immunotherapy and this was going to be the be-all end-all and I will admit I was amongst the believers. It looks no better than immunotherapy alone. (JB) Right. And I think that what we're finding as we do more of these studies, I think that if you look at clinicaltrials.gov and you look at combinations of PD-1 inhibitors in cancer… (JW) More than 3,000 say it's not. (JB) It's some frightening number. Unfortunately, not all of these studies are going to work. We need to be prepared to do the studies, identify what works, and follow the science to see what is helping, but we can't just rely on the early phase studies.

(JB) Recently, last year I think even, we spoke about Epacadostat. (JW) It looked so exciting last year. (JB) Looked so exciting; had a doubling of the expected response rate, but recently the study in melanoma which is a very big study combing Epacadostat with Pembrolizumab, did not find any improvement with the addition of Epacadostat. The study was halted and really most of the associated studies that had developed as a result of the excitement about these early phase studies including in head and neck cancer were halted as well.

(JB) So, there's reason to try to improve the outcomes, but I think we have to be cautious as we do thing and not get ahead of ourselves. (JW) I think that's right.

http://cancergrace.org/lung/2018/07/31/asco-2018-roundtable-head-and-neck-cancer-advances-in-immunotherapy-in-head-and-neck-cancer/