cancer NEWSLINE

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>> Welcome to Cancer Newsline. Your source for news on cancer research, diagnosis, treatment, and prevention. I'm your host, Dr. Oliver Bogler. Our guest is Dr. Michael Davies, Associate Professor in Melanoma Medical Oncology and we'll be talking about melanoma when it metastasizes to the brain. Dr. Davies, please tell us about current therapies for melanoma. I understand that conventional chemotherapy is not always effective. So can you tell us a little bit about what is being developed?

>> Yeah, thank you very much Oliver. Yeah, it's really interesting that historically melanoma has been one of the diseases where chemotherapy is really least effective. And that has really driven lots of research over the last decade to develop new, more effective therapeutic approaches. And really, the treatment of melanoma has been revolutionized in the last five years with new targeted therapies and immune therapies. One of the challenges in the development of all these agents, though, has been the treatment of patients with melanoma that has spread to the brain -- or brain metastases. This is actually one of the most common complications we run into in patients with stage four or metastatic melanoma, where historically up to 60% of patients with metastatic melanoma have developed brain metastases. Unfortunately, many clinical trials historically have excluded patients with brain metastases, but in recent years, the investigators in the community have really transformed trials to now actually have trials specifically for patients with brain metastases. And with those trials, we are really seeing exciting results with the new therapies.

>> So you mentioned targeted therapies. Can you give us some examples?

>> Yeah. So, in melanoma, approximately 50% of patients have a mutation in the BRAF gene. And so now, for any patient who is diagnosed with metastatic melanoma, we do testing to see if that mutation is present. If the BRAF mutation is present, there are several targeted therapies, which are pills that patients take once or twice a day, which are very effective at attacking the cancer cells. Those treatments actually can cause reduction in tumor size in up to 70% to 80% of patients that have the BRAF mutation. Unfortunately, they don't work for patients that don't have the BRAF mutation. One of the exciting things we found is that these treatments can be very effective even with melanoma has spread to the brain.

>> Is testing for that BRAF mutation you mentioned routine?

>> So, testing for that mutation is absolutely routine for patients with metastatic melanoma. And due to an increasing number of clinical trials for patients with earlier stage disease, we're starting to see testing for that mutation done in more and more patients every day.

>> Now, there's been a lot of excitement in some cancers with new immunotherapies, where the immune system is activated. Is there anything for melanoma in that area?

>> Absolutely. And again, historically, because this cancer didn't respond to chemotherapy, this was one of the earliest diseases in which we really investigated immune therapy as a new strategy to control cancer. Again, what this approach takes advantage of is the fact that we all have an immune system that is designed to defend our body against foreign invaders or other problems -- particularly, infections. But it appears that the immune system is also there to battle cancer. The question has been: Why does that defense system break down in patients with cancer? And more importantly, how can we reinvigorate the immune system to recognize and attack the disease? And melanoma has really been at the leading edge of immunotherapy research. Indeed, one of the very first treatments that was approved for melanoma in the 1990s was high dose interleukin-2, an immune therapy that stimulates the immune system and results in cures in approximately 5% of patients with metastatic melanoma. However, it is actually one of the most dangerous therapies that we give and has to be given in an intensive care unit setting. However, what we've seen over the last few years are new checkpoint inhibitor immune therapies, which are given as IV treatments on an out-patient basis every two to three weeks, which actually appear to be achieving durable disease control in anywhere from 30% to even 50% of patients with metastatic melanoma. That being said, immune therapy for brain metastases is quite challenging because the way that immune therapy works is by causing the immune system to attack the cancer cells which causes inflammation. In many parts of the body, that doesn't cause problems, but actually an inflamed tumor can actually cause side effects if that tumor is in the brain.

>> You mentioned checkpoints. What is that exactly?

>> Checkpoints are a new strategy that we have for activating the immune system. Just as an analogy, interleukin-2 was sort of the equivalent of pushing the accelerator on the car to activate the immune system. What our new immune therapies do -- the checkpoint inhibitors -- is sort of the equivalent of pulling off the brakes. And so ipilimumab was the first checkpoint inhibitor was approved in 2011 and then two anti-PD1 antibodies, which are another type of checkpoint inhibitor, were approved for patients in 2014 with pembrolizumab and nivolumab. And we're now entering the era of having clinical trials with those agents in patients even with brain metastases.

>> Lastly, talking about a more, sort of old standby therapy -- radiation therapy, which has been around a long time -- I understand there have also been some advances in this regard for melanoma patients with brain mets. Is that true?

>> Absolutely. So, historically, the way that we used to treat patients with brain metastases was whole brain radiation therapy. This was a way to provide radiation to other tumor cells, but actually had, as a downside, that it would radiate the normal brain tissue as well. Over the years, we've developed much more sophisticated ways of providing radiation through focused approaches that really aim high intensity radiation at the tumors without doing damage to the normal brain. And so called stereotactic radiation surgery, or here at MD Anderson, what we call the gamma knife treatment. And this therapy is very effective at controlling the brain metastases. We're actually now really interested in exploring whether that therapeutic treatment can be combined with the targeted therapies and the immune therapies to improve patients -- in patients with brain metastases for melanoma.

>> Dr. Davies, thank you very much for sharing your knowledge with our listeners.

>> Thank you very much. It was my pleasure.

>> For more information, visit MDAnderson.org. Thank you for listening to Cancer Newsline. Tune in for the next episode in our series.

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