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**Omid Hamid, MD**

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## Omid Hamid, MD, on Trailblazing Research in Melanoma

“You have to be on your game continually, you have to continually self-evaluate, and the field moves quickly.”

**N**ovel immune checkpoint inhibitors and adoptive T-cell therapies have dramatically changed the treatment landscape in melanoma over the past several years. Moreover, many treatments originating in the melanoma field also have been successful in other solid tumors. Future advancements, such as T cell–manipulative therapies, promise to expand the armamentarium available to clinicians.

In an interview with *ONCOLOGY*®, Omid Hamid, MD, discussed the trailblazing research at the Angeles Clinic and Research Institute in Los Angeles, California, and promising advances in melanoma more generally. He explored the profuse diversity of available treatments and the challenging rigor of clinical research. Additionally, Hamid provided an overview of the prospects for future developments in this treatment landscape.

**Q:** Which approved treatments for melanoma have you or your colleagues worked with as part of a clinical trial?

**HAMID:** [I've worked with] ipilimumab [Yervoy], nivolumab [Opdivo], tebentafusp-tebn [Kimmtrak], lifileucel, and the Instil Bio drug ITIL-168. [I was also involved with the] first trial to publish data on MK-3475, which became lambrolizumab and then pembrolizumab [Keytruda]. We [at the Angeles Clinic] have examined all the PD-1 targeting antibodies, including nivolumab, avelumab [Bavencio], durvalumab [Imfinzi], atezolizumab [Tecentriq], and pembrolizumab, in phase 1/2 clinical trials focused on melanoma, lung, and

similar solid tumors. We've also been building out our oncolytics program.

Notably, developments in melanoma will now trickle out into other solid tumors. The successes of mass-produced adoptive T-cell therapies [in melanoma] mean they will play a larger and larger role in multiple solid tumors, including head and neck tumors, cervical cancer, lung cancer, and others. [They will follow] the same path as immune checkpoint inhibitors in solid tumors.

**Q:** Why has melanoma research been a trailblazer for so many years?

**HAMID:** It's necessary to get buy-in from the community at large [when conducting research]. Additionally, because of the significant immunogenicity of melanoma, the magnitude of response [seen with some of these agents] allows us to venture into other solid tumors where the response may not be as great but where we can nonetheless move our understanding forward. Response rates with single agents in melanoma are lower [than those with combinations], and so we're developing combination regimens for this disease [that may also] improve outcomes in other solid tumors.

On the other side of the coin, [there can be] intense toxicities [with these agents] because the dosing regimens are intense. Those of us working in melanoma have learned from this, and so we've also been trailblazers in dealing with immune toxicities.

**Q:** What do you enjoy about working in clinical trials?

**HAMID:** It's hard to maintain the appropriate scientific rigor [in clinical trials] when you have a large staff. Everything has to be precise, and you have to be willing to submit your clinic to review. [For instance], we've been audited multiple times by the FDA to allow us to move drugs into approval. Trials we've performed have led to the approval of many drugs, and [consequently] the FDA has reviewed our clinic and found that we do phenomenal work, but this represents a huge amount of excess labor at a time when there's a physician crunch. That's what makes clinical research so difficult. You have to be on your game continually, you have to continually self-evaluate, and the field moves quickly.

The field of oncology is somewhat like the field of hematology—it's so dynamic that you can't just read up to a point and stop because you'll go to sleep and tomorrow there will be more to know. It's a constant enterprise [requiring] a mastery of these solid tumors.

I'm very happy to be part of my clinic because we've moved away from relying on a single person to know everything. [Instead, we've moved] toward a clinical system [relying on] many experts, not just in solid tumors but also in specific types of treatment processes. For example, in the field of lung cancer there are experts in chemotherapeutics, experts in targeted therapies and targeted therapy resistance, and experts in the new field of immunotherapeutic positions. All of these subfields necessitate significant expertise.

**Q: What do you think about optimal treatment planning in melanoma?**

**HAMID:** The major phase 3 clinical trials help us understand how to line up these therapies and the optimal order in which patients should receive them.

Moreover, we'll hopefully expand our understanding of predictive and prognostic markers, whatever they might be—PD-1 or PD-L1 staining, mutational burden, microbiome analysis, [or even] the time of day when treatment is given. This can make you want to hit your head against a brick wall because these answers can only come from the rigor of clinical trials and from collaboration.

[Speaking of which], that's the most rewarding non-patient care aspect of my job: being part of a like-minded community of people from around the world whom you enjoy as friends and collaborators. It's a very special community. I started out as a student and then eventually became an apprentice to Jeffrey Weber, MD, PhD. Now I come once a year and sit at the [18th Annual International Symposium on Melanoma and Other Cutaneous Malignancies®] as a colleague and learn at the feet of masters. We all recognize the limited amount of time we have, and so a meeting like this symposium serves as a massive download of advancements, standards, thought processes, and collaboration.

**Q: What are we learning about adjuvant vs neoadjuvant care? Have any recent data changed your thinking?**

**HAMID:** [Recent data] haven't changed our thinking as a community, but [the data have] lent credence to the fact that relapse-free survival is the wrong signal [to rely on]. We still need to know about combinations as they relate to other combinations through upcoming trials like the phase 3 NADINA [NCT04949113] trial. Neoadjuvant therapy is only [appropriate] for bulky stage III disease. Adjuvant therapy is still the standard of care for all patients, especially those with high-risk stage II and early stage III disease who aren't candidates for neoadjuvant therapy.

**Q: Looking over the past year, which trials have been most interesting, and are there any results you're excited about?**

**HAMID:** The data coming from Iovance-sponsored trials and others examining adoptive T-cell therapy, taken together with some of the data on tebentafusp or the new PRAME [preferentially expressed antigen in melanoma]-targeted agents, confirm what we knew [about these agents].

After checkpoint inhibitor therapy, we're looking to use T-cell manipulative therapies, some of which are coming down the pike and already available through clinical trials. This enables us to help patients who become resistant to checkpoint inhibitors by allowing us other treatment pathways to explore.

We're only at the beginning. There are many therapies being developed and refined. [For example], clinicians are refining the administration of adoptive T-cell therapy, adjusting either the conditioning, the interleukin stimulus, or the T cells themselves. There are also other agents [being developed] that manipulate the microbiome, or the tumor microenvironment. We still need more intelligence on this modality.

**Q: Given the near-infinite number of variables and treatment combinations, how do you design trials to maximize their usefulness?**

**HAMID:** I build programs offering multiple options for patients [to eliminate the need for] repeated, similar trials. I also try to target multiple arms of the immune system. It's also important to continually expand your knowledge base to act as a resource for your patients, rather than just enrolling them on trials without insight into their disease process. ■