

From COVID-19 to Melanoma? The Bright Future of mRNA Vaccines

The BNT111-01 clinical trial explores an mRNA melanoma vaccine on its own and in combination with a PD-1 checkpoint immunotherapy.

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Vaccines play an important role in keeping us healthy by protecting us from getting sick or by reducing the severity or duration of an illness. In addition to these preventive vaccines, researchers are also working to develop vaccines that treat disease, including melanoma, known as therapeutic vaccines. One researcher who is leading this charge is Dr. Adil Daud, professor and co-director of the Melanoma Center at the University of California, San Francisco (UCSF). Daud is the Principle Investigator of the BNT111 trial at UCSF. The trial is evaluating the effectiveness of BNT111, the lead candidate in BioNTech's mRNA melanoma vaccine program.

Therapeutic vaccines for melanoma are not a new idea. In fact, the first vaccine clinical trials in melanoma took place in the 1970s and have remained an active area of research ever since. Despite this long history and clinical promise, success for patients has been limited.

However, armed with the same Messenger RNA (mRNA) technology that made its widespread debut in several COVID-19 vaccines, such as those by Pfizer-BioNTech and Moderna, Daud and other researchers are finally hoping to turn this promising science into survival for patients.

"The thinking goes that traditional vaccines [in melanoma] that rely on proteins and peptides failed because they weren't able to spur a potent enough immune response," said Daud. "With mRNA vaccines, we hope to cut through the immune system clutter to create a robust immune response against melanoma."

The BNT111-01 Clinical Trial

Daud at UCSF — and 58 other sites across the globe — are currently enrolling patients in a Phase 2 clinical study testing BNT111, BioNTech's mRNA melanoma vaccine, in combination with cemiplimab, a PD-1 checkpoint immunotherapy, or as single agents for patients with Stage 3 or 4

melanoma who have been previously treated with a PD-1 based checkpoint immunotherapy. [Learn more about the BNT111-01 clinical trial!](#)

Dr. Paolo Ascierto, director of the Unit of Melanoma, Cancer Immunotherapy and Innovative Therapy at the National Tumor Institute Fondazione G. Pascale in Naples, is the global coordinating Principle Investigator for the study. For him, a working cancer vaccine has been a longtime coming. “The possibility of using an anti-cancer vaccine is one of the oldest wishes of all immuno-oncologists,” said Ascierto.

The BNT111 vaccine is made up of key mRNA sequences that teach your body how to make copies of four different antigens — or immune system triggers — that are found in melanoma (but not healthy cells). These antigen building instructions, completely harmless on their own, help to train the immune system to identify and seek out melanoma.

“For the same reason that researchers saw such great responses to the mRNA-based COVID-19 vaccines in comparison to some of the traditional approaches, we hope to see significant boost to the immune system’s response to any signs of melanoma,” said Daud.

Eligibility for this, and many other clinical trials, is exact: “I always tell my patients that when you consent to a study, you are agreeing to be screened. Unfortunately, there are many guardrails that limit who can be treated as part of a study,” says Daud. “What investigators want is to enroll patients who stand to benefit the most from participation while also doing everything we can to keep them safe. Generally, this is for people who despite their melanoma are otherwise in good health.”

After the consent and screening period, eligible patients will be randomized into three distinct arms:

- BNT111 monotherapy,
- Libtayo (cemiplimab) monotherapy, or
- BNT111 + Libtayo (cemiplimab) combination therapy.

“The advantage of this design is that when the trial is complete, we’ll really be able to tell if the vaccine is driving the treatment or if a combination is required,” says Daud. “For participants who are randomized into either of the monotherapy arms, should their melanoma progress, they’ll be given the option to join the combination arm as well. This is a nice patient-friendly feature of the [BNT111-01] trial.”

This Phase 2 trial is based on promising results from the Phase 1 Lipo-MERIT dose escalation trial ([NCT02410733](#)) that demonstrated BNT111’s favorable safety profile in 115 patients with melanoma. In addition, the experimental vaccine generated durable responses, as a single agent and in combination with a PD-1 based checkpoint immunotherapy. “The results, published in the medical journal Nature, give us confidence in the scientific merit of expanding study of BNT111

into a wider patient population,” says Daud.

Clinical Trials Are Critical to Advancing Research

[Clinical trials](#) are research studies that offer patients access to experimental treatment approaches that may prove more beneficial than anything currently approved by the FDA. In addition, clinical trials drive our understanding of melanoma forward, improving future treatment options for all patients. Lack of enrollment in clinical trials is one of the biggest obstacles to making new therapies widely available.

“I urge all my patients to look at clinical trials, especially those who didn’t respond to their first treatment, says Daud. “Clinical trial participation benefits patients because you have an entire team of medical professionals looking out for you. You get superior care because you are so closely monitored and that gives you a higher likelihood of success.”

Ascierto agrees: “A clinical trial is always an extra weapon for both the oncologist and the patient. The scrupulousness with which the studies are carried out, both in the attention paid to safety and efficacy, in some cases make the choice of the clinical trial the first therapeutic option for a patient. Patients should know that it could be a life-changing choice.”

MRA has developed many resources to help you [understand how clinical trials work](#), the potential [benefits and risks](#), [question to ask your doctor](#), and our [Clinical Trial Navigator](#) to help you find trials that may be right for you.

“Ten years ago, the folks who took part in the checkpoint immunotherapy clinical trials not only helped themselves, they’ve helped transform the way we treat melanoma and many other cancers,” says Daud. “That’s the power of clinical trial participation.”

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