Melanoma Cancer Clinical Trials to Watch

These clinical trials are designed to test new treatment approaches, help advance melanoma research and more.

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Treatment of advanced melanoma has dramatically improved over the past decade with 17 new therapies approved by the Food and Drug Administration (FDA). Even with these treatment advances, 50% of patients with advanced melanoma will either not respond to any of these treatments or their disease will progress, creating a critical need to find new therapies. In addition, approved therapies are not as effective in patients diagnosed with rare sub-types of melanoma - such as acral, mucosal and uveal - creating additional critical need for this group of patients.

Clinical trials are designed to test new treatment approaches, help advance melanoma research, and aim to improve future treatment options so that all patients may benefit. Lack of awareness of and participation in clinical trials are the biggest obstacles to bringing new therapies to market. MRA's Melanoma Clinical Trials to Watch series aims to raise awareness of clinical trials by regularly highlighting trials that are currently recruiting patients and featuring others that have recently shared promising updates for all sub-types of melanoma.

TILVANCE 301, A Phase III Clinical Trial for Melanoma Patients with Untreated, Unresectable or Metastatic Disease: Actively Enrolling

You may have heard of AMTAGVI, also known by the generic name lifileucel, a new therapy that recently earned FDA approval. AMTAGVI is a type of cellular therapy that uses Tumor Infiltrating Lymphocytes (TILs) to treat patients with advanced melanoma whose melanoma hasn't responded – or quit responding – to PD-1 based immunotherapies and BRAF/MEK targeted therapy, if their melanoma has the BRAF mutation. TIL therapies involve extracting immune cells called lymphocytes from a patient's tumor, growing them in a laboratory, and then reinfusing them back into the patient's body. TIL therapies aim to harness the patient's own immune system to target and destroy melanoma cells.

PD-1 therapies such as pembrolizumab, a type of immunotherapy called an immune checkpoint inhibitor (ICI), are approved for the treatment of advanced melanoma in the upfront or treatment-naïve setting. Pembrolizumab is an antibody that binds to a protein (PD-1) on the surface of immune T cells, releasing the brakes on T cells so that the immune system can attack and kill

cancer cells.

Clinical trials have been investigating the efficacy and safety of combining the cellular therapy, lifileucel, with pembrolizumab in patients with untreated, unresectable, or metastatic melanoma. Results from Phase II clinical trial IOV-COM-202 Cohort 1A, testing this combination in advanced melanoma patients who had not received prior ICI-treatment, demonstrated that two thirds of patients responded with almost a third of the patients having a confirmed complete response (total disappearance of tumor).

These encouraging Phase II results provided the rationale to open TILVANCE-301, a Phase III randomized clinical trial looking at the efficacy and safety of lifileucel in combination with pembrolizumab compared to pembrolizumab alone in untreated, unresectable, or metastatic melanoma patients. Patients meeting the eligibility criteria are randomized to one of the two arms (lifileucel + pembrolizumab or pembrolizumab alone). Participants whose disease progresses when receiving only pembrolizumab will be offered lifileucel monotherapy. This study is actively enrolling participants in the U.S., Canada, Australia, UK and several European countries. The trial also includes mucosal and acral melanoma patients who meet the eligibility criteria.

More information on the TILVANCE 301 trial is available. Please speak with your treating physician to see if this trial is right for you.

A Novel Radiotherapeutic Drug Approach Being Tested in Metastatic Uveal Melanoma Patients

Radiation emitted from different sources such as x-rays, gamma rays, electron beams, or protons has been used over many decades for the treatment of various cancers by killing and destroying tumor cells. One of the major limitations to this type of therapy is based on the way this treatment is delivered - as it may not only kill cancer cells, but also destroy the surrounding normal tissue. A more tumor-targeted approach has been developed through the emergence of radiopharmaceuticals, drugs that direct radioactive forms of chemicals called radioisotopes specifically to tumors, decreasing the risk of normal tissue damage with the ability to more specifically kill tumor cells. Depending on the type and energy of radiation emitted by the radioisotope, a higher dose of radiation may be delivered to the tumor with the potential of increasing the effectiveness and specificity of this type of treatment approach.

In 2016, Dr. David Morse (Moffitt Cancer Center) and colleagues received a Melanoma Research Alliance Team Science Award to test the activity of a radiopharmaceutical drug approach for uveal melanoma in preclinical uveal models. They attached a radioisotope called Actinium-225 to a drug that they designed, Ac-225-MTI-201, that is specifically targeted to and taken up by uveal melanoma cells. Studies in mouse models of uveal melanoma showed significant tumor growth delay and improved survival after treatment with Ac-225-MTI-201. These results led to the current first-in-human trial testing Ac-225-MTI-201 in metastatic uveal melanoma patients.

The Phase I trial, sponsored by Modulation Therapeutics and currently open at Moffitt Cancer

Center in Tampa, Florida, is testing different dose levels of Ac-225-MTI-201 to look at safety and tolerability of the drug. Metastatic uveal melanoma patients with progressive disease after at least one prior systemic or liver-directed therapy are eligible and receive a single administration of one dose level of Ac-225-MTI-201 by intravenous injection. Early assessment data presented at the September 2024 European Society of Medical Oncology meeting showed that single administration of a dose up to 76µCi appears safe and tolerated with stable disease reported in a few treated patients.

You and your clinician can find additional information about this trial.

New Trial Testing Oncolytic Virus Treatment in Patients with Acral and Rare Melanomas

A new clinical trial has opened that is focused on patients with acral melanoma, and rare melanomas, testing a new oncolytic virus drug, called BS006 (or oHSV2-PD-L1/CD3-BsAb). A Phase 1, multi-center, open-label, dose escalation trial of BS006 has opened and will be followed by a larger dose expansion study that is planned. Currently, two sites in Florida and Michigan are open and recruiting patients, with the plan for three additional recruiting sites (NCT05938296).

BS006 shares some similarities to approved oncolytic virus treatments. However, it has been engineered to hopefully be more potent at killing cancer cells. BS006 expresses an anti-CD3/anti-PDL1 bispecific engager antibody (called a BIKE). BS006 directly lyse (break down) tumor cells where it has been injected, and additional mechanisms of action include (2) the PD-L1/CD3 antibody that is expressed by BS006 could redirect T cells to kill tumor cells, and (3) relive the inhibitor effect on T cells and activate other immune cells.

BS006 is administered via intra-tumoral injection. The study will be conducted in two parts: both parts will consist of a screening period of up to 28 days, a treatment period, and follow-up period (safety and long-term follow up). The treatment period of Part 1 will include initial treatment period (3 doses of BS006) and an optional extended treatment period (repeated every 2 weeks). Subjects will be treated for up to 12 months.

Eligible patients have a solid tumor (such as melanoma) as detected by CT or MRI that have persisted, recurred, or metastasized despite therapy. Patients must have histologically confirmed advanced and/or metastatic melanoma, cutaneous squamous cell carcinoma, and other solid tumors with palpable, visible, or ultrasound detectable lesions.

Talk to your doctor to see if this clinical trial might be right for you. If your melanoma has not responded to initial treatment, or if you've had a progression of disease, recurrence, or metastasis, then you may be eligible.

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