Melanoma Skin Cancer Clinical Trials to Watch

The Melanoma Research Alliance shares research updates and highlights clinical trials for this skin cancer that are recruiting patients.

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By Joan Levy, Melanoma Research Alliance (MRA) Chief Science Officer

We are excited to begin the new year with MRA's Melanoma Clinical Trials to Watch series that aims to build awareness around 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. In this series edition, we highlight three trials that are currently recruiting patients.

Melanoma clinical trials are designed to test new treatment approaches, help advance research, and aim to improve future treatment options so that all patients may benefit. While the treatment of advanced melanoma has dramatically improved over the past decade with 17 new Food and Drug Administration (FDA) approved therapies, there is still an urgent need to find new therapies for the 50% of patients whose melanoma does not respond to currently approved therapies or progresses after treatment. In addition, currently approved therapies are not as effective in patients diagnosed with rare sub-types of melanoma, such as acral, mucosal and uveal. Clinical trials are essential in advancing new treatments so that all melanoma patients may one day benefit from different treatment options.

New Oncolytic Virus Combination Being Tested in Metastatic Uveal Melanoma

Uveal melanoma is a rare form of melanoma that occurs in certain tissues of the eye accounting for only 5% of all cases of melanoma in the United States. Up to 50% of patients with uveal melanoma will develop disease that spreads --or metastasizes-- to other tissues and organs, with the liver being the most common site of metastasis. Uveal melanoma has limited treatment options and generally is not very responsive to immune therapies.

A distinct type of immunotherapy using an oncolytic virus called RP2 is being clinically tested in metastatic uveal melanoma patients that have not received immune checkpoint inhibitor therapy. Oncolytic viruses kill tumor cells and modify immune cells in the tumor microenvironment to elicit an anti-tumor immune response when injected directly into tumors. Because the stimulated

immune cells circulate throughout the body, the anti-tumor effects are not only seen in the injected tumors but can spread systemically to non-injected tumors elsewhere in the body, commonly known as the abscopal effect.

Replimune's RP2 oncolytic viral therapy is based on a proprietary strain of herpes simplex virus that has been genetically engineered to express proteins that enhance tumor killing and have the potential to induce an anti-tumor immune response throughout the body. It is being evaluated in a Phase 2/3 randomized clinical trial (RP2-202) in which immune checkpoint naïve metastatic uveal melanoma patients either receive RP2 in combination with the immune checkpoint inhibitor, nivolumab, or a combination of the immune checkpoint inhibitor, ipilimumab and nivolumab. RP2 is administered by direct injection into the tumor.

The RP2-202 clinical trial has three different parts: 1) Screening up to 28 days to determine whether patients can be included in the trial and if so, then randomized into the RP2 + nivolumab group or the ipilimumab + nivolumab group (approved standard treatment for advanced melanoma; 2) Treatment period of up to approximately 2 years; and 3) Follow-up period of up to 3 years after treatment is completed.

An earlier Phase I trial tested RP2 alone or in combination with nivolumab in 17 metastatic uveal melanoma patients including those with both liver and other types of metastases. Data from this Phase I study presented at the annual American Society of Clinical Oncology (ASCO) conference in June 2024 suggested that RP2 alone and in combination with nivolumab had a favorable safety profile and an overall response rate or ORR (indicating tumor shrinkage) of 29.4% in this historically difficult-to-treat patient population. Further characterization of the tumor and immune cells of patients treated with RP2 plus nivolumab indicated that there were changes associated with immune cell activation. The encouraging data from this Phase I study provided the rationale to design and open the RP2-202 randomized trial.

Approximately 280 patients are expected to be enrolled in RP2-202 trial, and it is currently open in the U.S. Find out more information about this trial.

Now Enrolling Advanced Untreated Melanoma Patients to the PRISM-MEL-301 Phase 3 Clinical Trial

The PRISM-MEL-301 trial is testing an investigational drug, IMC-F106C, in combination with the immune checkpoint inhibitor, nivolumab, in patients with advanced melanoma that have not received any treatment for their disease. IMC-F106C is a class of immunotherapies that works by bringing together tumor and immune T cells, which help the body's immune system locate and kill the cancer cells. One part of this drug recognizes a marker called HLA-A*02:01 that binds to a specific protein called PRAME that is found in melanoma cells. The second part of IMC-F106C recognizes a protein expressed by immune T cells, creating a bridge between melanoma cells and T cells allowing the immune system to attack and kill the melanoma cells.

Not all patients have the HLA-A*02:01 marker that IMC-106C needs to recognize and bind to on

melanoma cells. That is why - in addition to being an untreated advanced melanoma patient - patients must also be screened to see if they have the HLA-A*02:01 marker. Therefore, patients must be tested to see if they are positive for this marker to determine eligibility for the trial.

If a patient meets the eligibility criteria of this trial, the study has 2 stages. If a patient participates in Stage 1, they will randomly be assigned to 1 of 3 groups.

- Group 1 receives a lower dose of IMC-F106C plus nivolumab
- Group 2 receives a higher dose of IMC-F106C plus nivolumab
- Group 3 does not receive IMC-F106C but instead receives either nivolumab alone or nivolumab with another checkpoint inhibitor called relatlimab

After 90 patients join and are treated in Stage 1, medical experts will look at the data and determine whether to pick the lower or higher dose for the second stage of the study. If a patient participates in Stage 2, they will be randomly assigned to either:

- The selected study dose of IMC-F19=06C and nivolumab
- Nivolumab alone or nivolumab and relatlimab

If a patient joined the trial in Stage 1 and is receiving the study drug dose that was not selected by the medical experts for Stage 2, they may be able to switch to the selected Stage 2 study dose if they and the study doctor agree to the change.

If a patient is eligible to participate, they will participate in the study for about 2 years and then undergo a follow-up period so that the doctor and study team can monitor their health.

Find additional information about this trial.

New Engineered IL-2 Drug Being Tested in a Phase 1 Study in Advanced or Metastatic Cutaneous Melanoma

High dose IL-2 (HD IL-2), also known as aldesleukin or PROLEUKIN, is an FDA approved immunotherapy that can produce long-term remission in patients with metastatic melanoma, including when standard of care treatments such as immune checkpoint inhibitors no longer work. HD-IL2 is administered systemically and works by increasing the growth and activity of immune cells called T and B lymphocytes throughout the body that in turn can then boost the immune system to fight and destroy melanoma. Despite the possible anti-tumor benefits, HD IL-2 can cause potentially life-threatening toxicities and patients receiving this treatment need to be hospitalized for several days to receive each cycle of therapy. Furthermore, patients are required to have an optimal clinical performance status - which is indicative of the patient’s ability to

perform certain daily living activities without the help of others, as well as having normal cardiac and pulmonary function - to receive treatment.

To try to harness the clinical benefits of IL-2's ability to fight melanoma but with less toxicity, Werewolf Therapeutics has engineered an INDUKINETM molecule called WTX-124 that is administered systemically but preferentially releases IL-2 within tumors rather than elsewhere in the body. The active ingredient in WTX-124 is the same form of IL-2 that has been proven to be clinically active when given as part of the HD IL-2 regimen.

WTX-124 is presently being studied in a Phase 1/1b clinical trial and there are opportunities for patients with advanced or metastatic melanoma to participate. In the trial, WTX-124 is being administered to patients as a monotherapy or in combination with the approved immune checkpoint inhibitor, pembrolizumab, after progression on approved therapies.

The study is currently enrolling advanced or metastatic cutaneous melanoma patients in different centers across the U.S. Looking for more information about this trial?

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