Highlights in Melanoma Treatment Advances from ASCO 2026

Experts shared groundbreaking clinical research across cancer types at the American Society of Clinical Oncology (ASCO) Annual Meeting.

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Over the past decade, significant advances in melanoma research have transformed the treatment landscape, bringing 19 approved therapies to patients with melanoma.

These include:

- Immunotherapies such as immune checkpoint inhibitors, oncolytic viruses, bispecific T-cell engagers, and cellular therapy
- Drugs that target specific alterations in melanoma tumor cells (BRAFi, MEKi)
- Combinations of immunotherapies and targeted therapies

Most approved melanoma therapies are intended for patients with metastatic disease or disease that cannot be completely removed through surgery (unresectable). However, immune checkpoint inhibitors and a combination of BRAF and MEK inhibitors have more recently been approved to treat patients with melanoma following surgical removal of tumors, which is referred to as treatment in the adjuvant setting. Several of these treatments have also been evaluated in the neoadjuvant setting, which is treatment before the surgical removal of the melanoma.

Despite this progress, current approved therapies remain ineffective in nearly 50% of patients with melanoma, including those with rare melanoma subtypes (like acral, mucosal, and uveal melanoma) and melanoma of the central nervous system (such as brain metastases and leptomeningeal disease).

The 2026 American Society of Clinical Oncology (ASCO) annual conference showcased the continued momentum in melanoma research and the ongoing efforts to develop new treatment

options for all melanoma patients.

Here we provide important developments in melanoma treatment from ASCO 2026:

New Developments in Cellular Therapy for Melanoma

IMA203-101 Trial: Anzutresgene autoleucel, also known as anzu-cell, is a personalized T-cell therapy developed by Immatics that is a one-time cell therapy designed to help a patient's own immune system target and destroy tumor cells. T-cells are collected from patients and modified to carry a PRAME-directed T-cell receptor that recognizes HLA-A*02:01/PRAME on tumor cells. Results from a Phase IB subset analysis of this ongoing, multi-center, phase I/II trial evaluating anzu-cel in patients with advanced PRAME-positive solid tumors were presented by Dr. Diwakar Davar at the University of Pittsburgh Medical Center. Evaluated in this subset were patients with cutaneous melanoma, uveal melanoma, and other melanoma subtypes with advanced disease. The objective response rate (ORR), or percentage of patients whose tumors shrink or disappear, was 56% (50% in cutaneous melanoma and 67% in uveal melanoma), and broad systemic antitumor activity was observed across different metastatic sites. Results also showed that anzu-cel achieved a median duration of response of 14.6 months and median overall survival of 16.2 months across all melanoma subtypes. A major takeaway from the IMA203-101 trial is that anzu-cel is a well-tolerated, clinically meaningful therapy for patients with advanced PD-1-relapsed melanoma. A randomized phase III SUPRAME trial is underway (NCT06743126).

Phase II Trial of TIL Therapy for Metastatic Uveal Melanoma: Results from a phase II trial (NCT03467516) of tumor-infiltrating lymphocyte (TIL) therapy in patients with metastatic uveal melanoma was presented by Dr. Udai Kammula at the University of Pittsburgh Medical Center. TIL therapy uses a patient's own immune cells to fight tumor cells: lymphocytes are collected from a patient's tumor, grown into large numbers in the laboratory, and then reinfused back into the patient. This trial evaluated the efficacy of TIL therapy in patients with metastatic uveal melanoma and the use of a tumor biomarker called UMIS (Uveal Melanoma Immunogenomic Score) to predict TIL therapy response. The ORR was 22% with a median response duration of 10.8 months, with tumor-reactive TIL showing a higher response rate of 37%. UMIS identified tumors containing tumor-reactive TIL and was predictive of clinical outcomes, supporting its potential as a precision biomarker for selecting patients and tumors most likely to benefit from TIL therapy.

Phase II Trial of OBX-115 Engineered TIL Therapy: Dr. Allison Betof at Stanford University School of Medicine reported on a phase II trial (NCT06060613) evaluating the safety and efficacy of OBX-115 engineered TIL therapy in patients with advanced melanoma, including acral, cutaneous, and mucosal melanoma. OBX-115, developed by Obsidian Therapeutics, is an engineered TIL therapy expressing regulatable membrane-bound IL-15, designed to improve upon standard TIL therapy.

Potential advantages of OBX-115 include less invasive tissue procurement, low-dose lymphodepletion, and controlled TIL expansion and persistence. OBX-115 demonstrated encouraging early efficacy with a 67% overall response rate, the potential for durable and deep responses, and manageable side effects, positioning it as a promising new treatment option for patients with advanced melanoma.

Individualized Neoantigen Therapy as a New, Personalized Approach to Melanoma Treatment

KEYNOTE-942 Trial: Five-year follow-up data from the phase II KEYNOTE-942 trial (NCT03897881) was presented by Dr. Matteo Carlino from the Melanoma Institute Australia. Intismeran autogene, also known as intismeran, is an mRNA-based individualized neoantigen therapy developed by Moderna and Merck that helps the immune system recognize and attack tumor cells based on the specific mutations in a patient's tumor. The KEYNOTE-942 trial evaluated the use of intismeran plus pembrolizumab versus pembrolizumab monotherapy in patients with resectable stage IIIB-IV cutaneous melanoma. At five years of planned follow-up, intismeran plus pembrolizumab showed a 49% reduction in the risk of recurrence or death and a 59% reduction in distant metastasis or death compared to pembrolizumab alone. The combination therapy continues to show a favorable safety profile. Results from this follow-up analysis indicate that intismeran plus pembrolizumab may be a potential treatment approach for patients with resected, high-risk, advanced stage cutaneous melanoma. A phase III registrational trial of high-risk, resected, Stage II-IV melanoma has accrued all patients and is awaiting data readout.

Oncolytic Viruses as a Promising Therapeutic Approach in Melanoma

IGNYTE Trial: Dr. Michael Wong at Roswell Park Comprehensive Cancer Center presented 3-year data from the IGNYTE trial (NCT03767348) which evaluated RP1 plus nivolumab combination therapy in patients with advanced melanoma that progressed on PD-1 inhibitor therapy. RP1, developed by Replimune, is a novel oncolytic immunotherapy that uses a modified virus to attack tumor cells while also helping the immune system to better recognize and fight tumors throughout the body. This combination therapy showed extended overall survival benefits in patients with a 3-year overall survival of 32.9 months and a median overall survival rate of 47.8%. The overall survival rate was 83.5% among patients who responded to treatment. Results from this trial indicate the long-term clinical benefit of RP1 plus nivolumab in patients with advanced melanoma who have failed prior PD-1-inhibition therapy.

RP2-001-18 Trial: RP2, developed by Replimune, is similar to RP1 but is further modified to overcome suppression of the immune response by inhibiting the immune checkpoint, CTLA-4. First-in-human data for RP2 alone and in combination with nivolumab in patients with advanced solid tumors was presented by Dr. Joseph Sacco from the Clatterbridge Cancer Centre and University of Liverpool. Both RP2 monotherapy and RP2 in combination with nivolumab achieved

an ORR of 19.0% and 19.1%, respectively across all solid tumor types tested. In patients with uveal melanoma and cutaneous melanoma, RP2 achieved a 33.3% and 36.4% ORR, respectively in a pooled dataset of RP2 administered as a monotherapy and in combination with nivolumab. Uveal melanoma was one of four cancers that had a patient achieve a confirmed response (tumor shrinkage) to RP2 monotherapy. Overall, both treatment approaches were well tolerated, elicited a systemic immune response, and produced durable responses, notably in heavily pretreated patients. A randomized phase II/III trial evaluating RP2 in combination with nivolumab in patients with metastatic uveal melanoma is currently enrolling (NCT06581406).

Redefining Neoadjuvant Treatment Paradigms for Patients with High Risk, Stage II Melanoma

NeoReNi II Trial: Presented by Dr. Georgina Long from the Melanoma Institute Australia, the NeoReNi II trial (NCT05418972) evaluated the feasibility, response, and safety of checkpoint inhibitor neoadjuvant therapy (NAT)–referring to treatment before surgery–in resectable stage II cutaneous melanoma. Critically, this trial investigated a new treatment strategy for patients with stage II cutaneous melanoma, which is associated with a 40-50% risk of recurrence after receiving wide local excision surgery alone. In this trial, patients received neoadjuvant immune checkpoint inhibitors, nivolumab and relatlimab, followed by wide local excision surgery. Major pathological responses (the presence of ≤10% of residual viable tumor after neoadjuvant therapy) were observed in 65% of patients and recurrences post-surgery were observed in 15% of patients. The 12-month event-free survival was 89%, indicating that this percentage of patients did not experience progression pre-surgery, recurrence post-surgery, or death due to disease or treatment. Results from the NeoReNi II trial indicate this treatment regimen is feasible in high-risk stage II cutaneous melanoma with high response rates.

Progress in Potential Therapeutic Approaches for Rare Melanomas and Melanoma Brain Metastases

OptimUM-02 Trial: Dr. Marlana Orloff at Thomas Jefferson University Hospital reported on primary results from the OptimUM-02 phase II/III trial (NCT05987332), which is evaluating the safety and efficacy of darovasertib plus crizotinib as a first-line treatment in metastatic uveal melanomas that are HLA-A*02:01-negative. At the present,

no FDA-approved treatments exist for HLA-A*02:01-negative metastatic uveal melanoma patients. Darovasertib, or IDE196, is an oral targeted therapy developed by IDEAYA that works by selectively inhibiting the PKC protein that is overactive in most uveal melanomas. Darovasertib plus crizotinib improved progression-free survival (6.9 months versus 3.1 months) and ORR (37.1% versus 5.8%) compared with patients receiving investigator’s choice of treatment. Overall survival data are forthcoming. These results support darovasertib plus crizotinib as a potential new therapeutic approach for HLA-A*02:01-negative metastatic uveal melanoma.

First-in-human Trial of ^{225}Ac-MTI-201 in Metastatic Uveal Melanoma: Dr. Nikhil Khushalani from Moffitt Cancer Center presented final data from the phase I trial (NCT05496686) of the ^{225}Ac-MTI-201 radiopharmaceutical therapy developed by Modulation Therapeutics in patients with metastatic uveal melanoma. ^{225}Ac-MTI-201 works by delivering radioactive actinium-225 directly to tumor cells that express MC1R, a protein that is highly expressed by uveal melanoma cells. Single-dose administration of ^{225}Ac-MTI-201 with dose escalation was found to be safe and feasible in patients with metastatic uveal melanoma. Stable disease was observed in 27% of patients with a median progression free survival of 2.3 months. A multi-dose study of ^{225}Ac-MTI-201 in metastatic uveal melanoma is planned.

Updated CAP 03-NEO Trial Results in Acral Melanoma: Dr. Lu Si at the Peking University Cancer Hospital and Institute presented stage 2 data from the CAP 03-NEO two-stage trial (NCT05512481) which evaluated the efficacy and safety of a triple-drug regimen as a neoadjuvant, or pre-surgery, therapy in patients with resectable stage III acral melanoma. Patients received camrelizumab (anti-PD-1 antibody), apatinib, and temozolomide followed by surgery and adjuvant camrelizumab. At 12-months post-treatment, relapse-free survival and distant metastasis-free survival were 80.3% and 84.8%, respectively, and reflect the percentage of patients with no signs of cancer or are free of distant metastases. Pathological responses measured after neoadjuvant therapy were observed in 62% of patients. When compared with an external cohort receiving surgery and adjuvant PD-1 inhibitor therapy, the neoadjuvant triple-drug regimen demonstrated clinical benefit in patients with resectable stage III acral melanoma.

Phase I Trial of a Next-Generation, Brain-Penetrant BRAFi/MEKi in BRAF-mutant Melanoma: Treatment of BRAF-mutant melanoma has improved with BRAF and MEK inhibitors, however, such therapies have limited duration of benefit and reduced efficacy in brain metastases. Dr. Monica Chen at Memorial Sloan Kettering Cancer Center reported on an ongoing Phase I trial (NCT05538130) involving a next-generation combination therapy of oral, brain-penetrant BRAF and MEK inhibitors. Developed by Pfizer, claturafenib (PF-07799933) is a targeted therapy that inhibits BRAF-V600 and non-V600 mutants and polfurmetinib (PF-07799544) is a targeted therapy that reversibly inhibits MEK. The trial evaluated dose escalation and (DE) and dose optimization (DO) of claturafenib and polfurmetinib combination therapy. The DE phase enrolled patients with BRAF-mutant (V600 and non-V600) advanced melanoma and observed an ORR of 27%. The DO phase enrolled patients with BRAF-V600 mutant advanced melanoma and observed an ORR of 32%. For patients with brain metastases present at the start of the trial, the intracranial ORR, or antitumor activity of this combination therapy in the brain, was 30% in DE patients and 22% in DO patients. Overall, calturafenib and polfurmetinib had a manageable safety profile and demonstrated encouraging activity both systemically and in the brain in patients with advanced BRAF-mutant melanoma.

To learn more about melanoma clinical trials, visit curemelanoma.org/clinicaltrials.

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