Eyes Widen for Uveal Melanoma Treatment: Sapna Patel's Groundbreaking Findings at ESMO 2025

A PRAME milestone for uveal melanoma — a rare cancer of the eye — may pave the way for treating other tumors and boost cancer patient survival.

November 10, 2025 By University of Colorado Cancer Center and Megan Palffy

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In a major stride for cancer research, Sapna Patel, MD, a leading oncologist and researcher at the University of Colorado Cancer Center, presented transformative findings during the prestigious Presidential Symposium at the 2025 European Society for Medical Oncology Congress in Berlin in October. Patel's phase I trial targeting uveal melanoma — a rare and historically hard-to-treat eye cancer — has shown unprecedented promise, offering new hope to patients while reshaping the future of immunotherapy.

As the Dr. William Robinson Endowed Chair in Cancer Research at the CU Cancer Center and building on her work from her previous institution, Patel is researching a novel cell therapy called anzutresgene autoleucel (anzu-cel for short, IMA-203) that uses genetically engineered T cells to target a protein called Preferentially Expressed Antigen in Melanoma (PRAME). PRAME is highly expressed in over 50 types of solid tumors and is found in up to 90% of cases of uveal melanoma. This makes it an ideal target for T cell receptor therapy, which relies on the immune system's ability to recognize and attack cancer cells.

What makes PRAME unique is its journey through the cell. Although it's an intracellular protein, it gets processed and presented on the surface of cancer cells in the context of HLA molecules. This surface presentation allows the anzu-cel engineered T cells to recognize and bind to PRAME, initiating a targeted immune response.

"It's highly specific and personalized," Patel explained. "Every single one of the 16 patients in our trial showed some tumor reduction. I've never seen a response like that in my 20 years of treating uveal melanoma."

Why PRAME matters

Unlike other mutations that remain hidden inside cells and are difficult for the immune system to detect, PRAME's surface presentation in the context of HLA proteins makes it accessible. Even more compelling, these antigens do not need to be mutated to be targeted. The therapy works against the normal variant, broadening its applicability and effectiveness.

This breakthrough is especially significant given the treatment options historically available for uveal melanoma. While skin melanoma has seen more than 20 drug approvals in the past 15 years, uveal melanoma has lagged.

"We've revolutionized skin melanoma treatment," Patel said. "But for uveal melanoma, we've only recently seen our first two FDA approvals."

Safety and efficacy: a promising start

As a phase I trial, the primary goal was to assess safety. The most common side effects were cytopenias related to the chemotherapy portion of the treatment and these were expected and manageable. Notably, while all 16 patients experienced some level of cytokine release syndrome, a known side effect of T cell receptor therapies which can cause fever, chills, nausea, headache, rash, low blood pressure and rapid heartbeat, it was mild and resolved in most patients within two weeks.

Importantly, there were no treatment-related deaths in the broader trial, and none among the 16 with uveal melanoma. The confirmed objective response rate was 67%, and all patients showed some degree of tumor reduction. "This is not just a safety win, it's a signal that the treatment works," Patel said.

Looking ahead: phase II and III trials

While the phase I results are exciting, Patel is quick to note that larger, randomized trials are needed to validate the findings. A phase III trial is already underway in skin melanoma, which also shows high PRAME expression. As skin melanoma is more common, it offers a practical path for broader validation.

However, Patel is committed to ensuring that uveal melanoma patients aren't left behind. A confirmatory phase II trial is being planned specifically for uveal melanoma, with select sites including the CU Cancer Center, chosen for their expertise in cell therapy and rare cancers.

"We want to make sure this signal doesn't get lost," she said. "We're writing the protocol now and preparing to open the trial soon."

Challenges and opportunities

One challenge is the therapy's restriction to patients with HLA-A*02:01, a genetic marker found in about 25% of the U.S. population. Screening for this marker is essential to identify eligible patients. But for those who qualify, the potential benefits are significant. "Even if the response rate drops to one-third in future trials, that's still a meaningful survival benefit," Patel noted.

Another advantage of the therapy is its one-time treatment model. Unlike many modern therapies that require ongoing administration for years, this treatment is delivered once in a hospital or outpatient setting, reducing the burden on patients and potentially improving quality of life.

A new era for rare cancers

Patel's work is not just a milestone for uveal melanoma; it could pave the way for treating other tumors that don't naturally stimulate strong immune responses. If this approach proves effective in uveal melanoma, it could be adapted for pancreatic, ovarian, and some brain cancers.

"This isn't just about one cancer," Patel says. "It's about unlocking the potential of T cell therapies for a whole class of hard-to-treat diseases."

As the CU Cancer Center prepares to join the next phase of this groundbreaking research, the excitement is palpable. "We're ready to catch fire with this program," Patel explains. And for patients with rare cancers, that fire could be a light at the end of a long tunnel.

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