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'An incredible opportunity'

Mimivax looks for game-changer in GBM as Survaxm shows signal at interim look

By Marie Powers, News Editor

Like David against Goliath, Roswell Park Comprehensive Cancer Center (RPCCC) spinout Mimivax LLC is seeking to take down one of the most common and aggressive forms of primary brain cancer, and interim findings from its U.S. multicenter phase II study suggest the Buffalo, N.Y.-based company may have a shot. Key Interim results of Survaxm, its survivin peptide mimic immunotherapeutic vaccine, showed that 91 percent of patients with newly diagnosed glioblastoma multiforme (nGBM) who received the treatment in combination with standard of care achieved 12-month overall survival (OS) compared to 61 percent historical standard of care. In addition, 96 percent achieved six-month progression-free survival (PFS) on the Survaxm regimen compared to 54 percent historical standard of care.

The study is small, with 63 participants enrolled, and results are preliminary, but the company is already eyeing a randomized trial pending a positive outcome for the phase II, expected to finish by year-end.

The cell survival protein survivin is present in 95 percent of individuals with glioblastoma and in those with many other forms of cancer. Invented at RPCCC, Survaxm offers dual mechanisms of action designed to stimulate a patient's T-cell immunity and inhibit the survivin pathway to control tumor growth and prevent or delay tumor recurrence. The therapy was granted orphan drug designation by the FDA in the indication.

The ability to stimulate T cells and antibodies at the same time "is a little unusual" as an immunotherapy approach, said Michael Ciesielski, CEO of Mimivax and assistant professor of neurosurgery and oncology at RPCCC.

"We have a cytotoxic T-cell response attacking the cell at the same time that we have an antibody that's specifically interfering with the survivin molecule," he explained. "We have two very different mechanisms of action generated from the same drug."

Specifically, Survaxm activates mid-affinity T-cell receptors to circumvent immune tolerance, stimulates durable multi-epitope CD8-positive and CD4-positive T cells as well as immunoglobulin G (IgG) production, and prompts intracellular and cell-surface target recognition. The 15 amino acid synthetic long peptide is coupled to native high molecular weight keyhole limpet hemocyanin, offering high-density peptide delivery.

Ciesielski is co-inventor of the technology, together with Robert Fenstermaker, chief medical officer of Mimivax and chair of neurosurgery at RPCCC. The company holds an exclusive global license to Survaxm, with multiple patents extending to 2033 and beyond

The single-arm nGBM trial enrolled individuals ranging in age from 20 to 82 years (median=60) who underwent craniotomy with gross total resection, followed by chemoradiation. Survaxm was delivered through a subcutaneous injection of four serial priming doses of (500 mcg) with montanide and sargramostim (100 mcg) every two weeks, followed by standard adjuvant temozolomide and maintenance Survaxm every 12 weeks until progression. Endpoints were designed to assess PFS at six months, OS at 12 months and immunologic response in nGBM patients treated with Survaxm.

In addition to the overall OS and PFS findings, 13 of the 63 patients enrolled in the study remained progression-free for more than 12 months. Survaxm was highly active in stimulating immunologic response against tumor cells and produced survivin-specific antibody (IgG) titers and CD8-positive T-cell responses. Survaxm also showed the capacity to stimulate immune helper cell support, needed to sustain antitumor CD8-positive activity.

The regimen was generally well-tolerated, and drug-related adverse events were mild, according to Ciesielski, who said more complete interim data will be presented at the American Society of Clinical Oncology annual meeting, which begins next week in Chicago.

'Very excited about the data'

The company's confidence in Survaxm has grown in tandem with the development program.

"We've gotten very excited about the data," Ciesielski told *BioWorld*. "Our phase I study was conducted almost five years ago, and patients from that study are still alive, which gave us optimism going into the phase II."

In the ongoing study, survival trends in the Survaxm arm have strengthened slightly as the data have matured. With the phase II in nGBM so far achieving a survival rate that exceeds the historical standard of care by 40 percent, rather than the targeted rate of 15 percent, the study already met the six-month PFS endpoint. Ciesielski is optimistic that mature OS data will be consistent with the interim findings when the study reads out near year-end.

"We honestly did not expect to see such a high survival rate," he said, so the interim findings "opened our eyes that we really had something very special on our hands. We want to move this forward and get it to patients as soon as we can."

Should Survaxm perform as expected, Mimivax expects to advance into a randomized phase II study with the potential for an accelerated approval pathway.

Mimivax – the name refers to its "mimic" of the survivin protein – is prepared to take Survaxm through a registration trial in GBM on its own. By tapping the resources of RPCCC, which fulfilled many of the functions of a CRO, Mimivax has stayed lean and capital-efficient. The company has raised $10 million since its inception in 2012, mostly in grants along with a $1.5 million series A, to support an executive team of five people and several lab employees. The company is in discussions with investment banks and venture firms about a series B to prepare for the next phase of Survaxm's development.

Mimivax is advancing Survaxm in GBM due to the knowledge of its founders about the indication. However, the company also is exploring the candidate in a phase I trial in combination with Revlimid (lenalidomide, Celgene Corp.) as maintenance therapy for adults with multiple myeloma and is open to partnerships that could pair the asset with checkpoint inhibitors and other immunotherapy agents targeting other tumor types. Checkpoints often are used to "take the foot off the brakes" and allow the body's immune system to assist in the defense against cancer, "but sometimes you forget to put gas in the tank," Ciesielski observed. "We hope Survaxm can provide that extra boost to the checkpoint inhibitors."

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Mimivax also is building a pipeline around its lead program. Its scientists isolated the proprietary anti-survivin antibody in its vaccine for potential development as an independent, passive immunotherapy. The company also developed a chimeric antigen receptor (CAR) T cell that targets solid tumors, "which could give us a leg up in that portion of the cancer world," Ciesielski said.

In addition, Mimivax is developing a diagnostic that can be used to monitor immune responses to the Survaxm antigen and, at the same time, assess whether tumors are progressing.

But the company's immediate focus is to "keep driving forward" on Survaxm in GBM, where Mimivax hopes to accrue data that are sufficiently compelling to attract a partner to take the asset to market, either through a licensing arrangement or M&A. Notwithstanding the dire history of drug development in GBM, "we've gotten a lot of interest from companies that are willing to look into the indication," Ciesielski said. Although GBM is a tough nut to crack, "at the same time, there's a completely unmet medical need, and there's actually an incredible opportunity there to try to make a difference in some of these patients' lives. We're actively working with pharmas willing to take that chance with us." ♦