Medicenna gains precedent-setting FDA approval to design a hybrid Synthetic Control Arm® for a Phase 3 registrational trial

Medicenna leveraged Medidata AI Synthetic Control Arm (SCA®) to bolster Phase 2 findings and gain FDA approval to design a hybrid external control arm for their Phase 3 registrational trial

Key Takeaways

- In Phase 2, the SCA enabled Medicenna to better understand the expected survival benefit for their treatment. This knowledge supported their proposed hybrid Phase 3 design.
- In a precedent-setting regulatory decision, the FDA agreed to consider the use of a hybrid SCA in Medicenna's Phase 3 registrational trial.
- In Medicenna's upcoming trial, the hybrid SCA will reduce the number of prospective control patients needed by approximately 2/3 or 100 patients. This design will give enrolled patients a greater chance to receive the experimental drug, easing recruitment, reducing control patient drop-out, and accelerating trial timelines without compromising the scientific interpretability of the trial.

Customer

Medicenna, a mid-sized clinical-stage immunotherapy company, is on a mission to combat the world's toughest diseases. Their therapies are proprietary interleukins, named Superkines, that can modify the body's immune system to combat diseases. One of Medicenna's most promising molecules is MDNA55, which uses a highly specific interleukin-4 receptor (IL4R) targeted therapy to treat recurrent Glioblastoma (rGBM).

Challenge

Glioblastoma is one of the most aggressive forms of cancer with very limited treatment options. Patients typically survive less than 15 months after first diagnosis and only 6-9 months following relapse.[1]

The nature of rGBM makes it extremely difficult to recruit and retain patients for study in a clinical setting. Patients may hesitate to enroll in studies due to the possibility of being placed in the control group requiring treatment with the standard of care. They may also drop out early upon learning they have not been assigned to the investigation therapy.

MDNA55 offers a promising opportunity to improve outcomes for this aggressive cancer. Because of the unique challenges in studying, treating, and conducting rGBM trials, Medicenna faced difficulties interpreting the results of their single arm Phase 2 study. The company needed to design a Phase 3 registrational trial that could successfully recruit and retain patients to demonstrate the effects of MDNA55 for registration.

1. https://www.medicenna.com/clinical-trials/recurrent-glioblastoma/

Solution

Medicenna selected the Medidata AI team to create an SCA to re-analyze their Phase 2 trial and better understand the treatment effect. An SCA uses patient data from past clinical trials instead of recruiting a new control group. It can provide a scientifically rigorous comparison in scenarios where a control group is hard to recruit or retain, such as rare or imminently life-threatening diseases where the standard of care can be considered inadequate.

Medidata AI used the results of the Phase 2 SCA analysis to design a hybrid SCA and statistical analysis plan for Medicenna's confirmatory Phase 3 trial to demonstrate the efficacy of MDNA55. This design reduced the number of prospective control patients needed by approximately 2/3 or 100 patients. Medidata AI and Medicenna presented this novel design to the FDA at an end-of-Phase 2 meeting.

> "Medidata AI literally rolled up their sleeves, helped us analyze the data, and suggested ways to improve our clinical trial design. They were essentially part of our statistical group... We worked with Medidata and leveraged that information when we went to the FDA."
> **-Dr. Fahar Merchant, President and CEO, Medicenna**

Results

The FDA agreed to consider the use of an SCA in Medicenna's Phase 3 rGBM trial. This was a precedent-setting regulatory decision to consider a hybrid external control (combining SCA patients with randomized patients) in a Phase 3 trial in an indication that previously used traditional 1:1 randomized controls.

In Phase 2, the SCA enabled Medicenna to better understand the expected survival benefit for MDNA55. This knowledge supported sample size calculations for the hybrid Phase 3 design.

In Medicenna's upcoming trial, the hybrid SCA will give enrolled patients a greater chance to receive the experimental drug, improving enrollment, reducing patient drop-out, and accelerating trial timelines without compromising the scientific interpretability of the trial. The FDA's acceptance of this unique design will expedite the trial timeline, giving patients hope and earlier access to MDNA55 for a disease with poor prognosis and high unmet need.

> "This first true apples-to-apples comparison of the data shows that a single treatment with MDNA55 has the ability to more than double the survival rates in patients with the most aggressive form of rGBM. We hope that these results are a watershed moment in the battle against this aggressive and fatal disease, and are particularly meaningful considering that even a modest 25% improvement in survival has not been demonstrated by any of the approved treatments of rGBM in more than two decades."
> **-Dr. Fahar Merchant, President and CEO, Medicenna**