Celsion Phase Ib Ovarian Cancer Study Shows Strong Progression-Free Survival Treatment Effect Using a Medidata Acorn AI Synthetic Control Arm®

Key Takeaways

- After conducting a single-arm Phase Ib study, Celsion wanted a fuller understanding of the treatment effect of GEN-1, their ovarian cancer treatment, to justify continued drug development.
- Celsion partnered with Medidata Acorn AI to create an SCA composed of historic clinical trial patients that were near-perfect matches for the characteristics of the GEN-1 Phase Ib patients.
- A comparison of GEN-1 patients to the SCA found that the treatment effect was substantial enough to justify further research in a randomized Phase II trial.
- The estimated treatment effect also informed the design of the subsequent Phase II trial. The trial required approximately 20 fewer patients than was previously estimated, reducing trial costs and accelerating drug development timelines.

Customer Challenge

Celsion is a mid-sized biopharmaceutical company that develops next-generation chemotherapy and immunotherapy agents for liver and ovarian cancers. One of their most promising therapies is GEN-1 – a cell transfection agent entraining persistent, local secretion of the interleukin-12 protein to stimulate the body's immune system to kill cancer cells.

Celsion needed to assess the efficacy of their new compound. Although GEN-1 showed impressive progression-free survival (PFS) among stage III/IV ovarian cancer patients treated neoadjuvantly in the Phase Ib dose-escalating OVATION I study, the study was single-arm. That is, it did not have a control arm to compare against the PFS estimate. Celsion could not estimate the comparative efficacy in GEN-1 with their trial data alone, leaving them unsure whether to continue drug development.

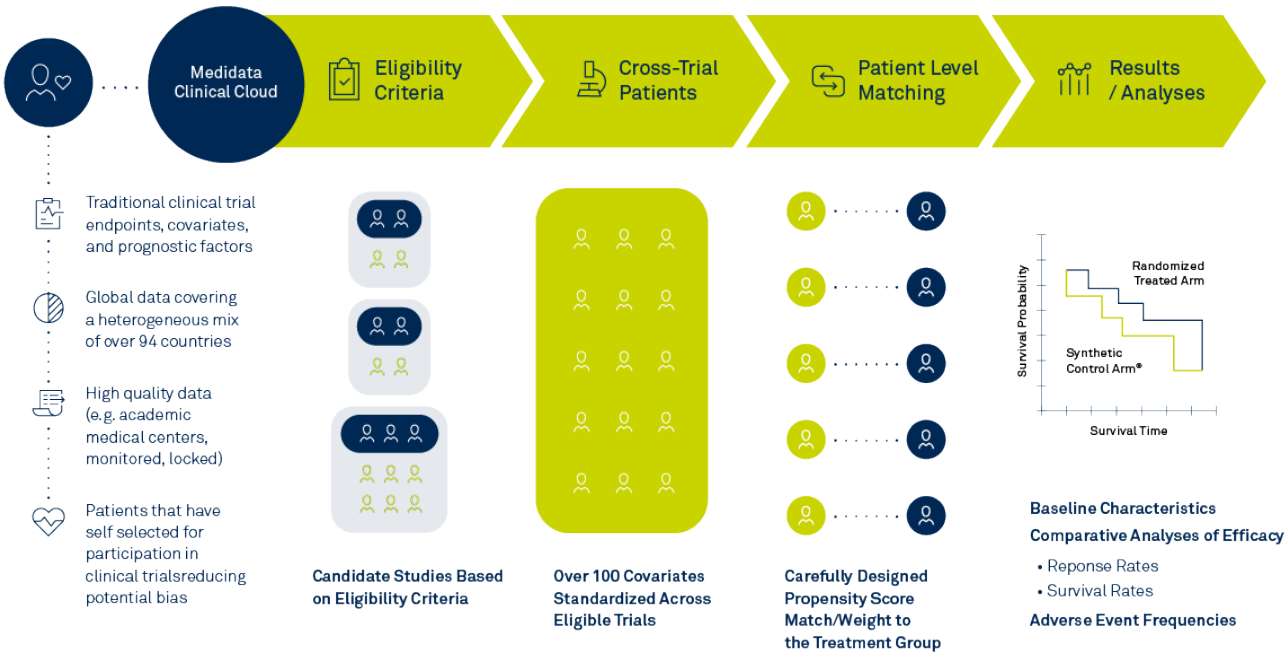
It is not uncommon for early phase trials to move forward without a control arm. In the traditional drug development paradigm, investigators often identify compelling agents through single-arm Phase II trials and study them against a standard of care control arm in larger subsequent Phase III trials.

Solution

Celsion partnered with Acorn AI to create a synthetic control arm (SCA) whose patients were a near-perfect match for the characteristics of the Phase Ib OVATION I patients. An SCA is a type of external control arm that uses patient data from past clinical trials instead of recruiting a new control group. It can provide a scientifically rigorous comparison in situations where a randomized control group is not available, especially in early drug development. Sponsors can use SCAs to gain a deeper understanding of the magnitude of treatment effect, helping them decide whether to continue drug development. At Acorn AI, we create fit-for-purpose SCAs our pool of more than eight million anonymized patients from 27,000+ previous clinical trials.

In Celsion's case, Acorn AI combed its robust database of historical clinical trials to find patients who otherwise resembled OVATION-I patients at baseline and were treated with standard of care therapy. The team used these patients to create an SCA that yielded comparative estimates of the benefit of adding GEN-1 to standard neoadjuvant treatment for advanced ovarian cancer. Acorn AI was able to create a control arm by matching these patients with the OVATION-1 patients in order to compare survival outcomes.

Historical Clinical Trial Patients from the Medidata Clinical Cloud have Distinct Advantages



Results

Acorn AI compiled an SCA that was a near-perfect match for the characteristics of the Phase Ib OVATION-I patients, and a comparison of the two groups suggested that GEN-1 was effective enough to justify further development in the Phase II setting. "It certainly convinced us that our drug had an effect," says Dr. Nicholas Borys, Chief Medical Officer at Celsion.

But the greatest value Borys sees currently is in helping to point development of all kinds of treatments in the directions most likely to be successful. "Right now, we really don't know if a drug is showing a benefit until we've given it to a few hundred patients," he says. "If we have an [SCA], we can get a pretty good signal with a fraction of those numbers." The SCA results led Celsion to plan a follow-up randomized Phase II trial requiring approximately 20 fewer patients than they estimated prior to the SCA. Taken together, the SCA may accelerate GEN-1's development with the ultimate goal of getting an effective drug to patients sooner.

> **"The Medidata Synthetic Control Arm provided reliable estimates of the efficacy endpoints, which allowed for a decrease in the number of patients needed to participate in the subsequent randomized Phase II trial. In addition to decreasing the burden on patients, this helped to accelerate trial timelines and decrease costs. This truly important progress will lead to further insights and advancements in future trials and, in the end, help bring treatments to patients faster." —Dr. Nicholas Borys, Chief Medical Officer at Celsion**