HOW NASHVILLE BIOSCIENCES CAN FACILITATE SYNTHETIC CONTROL ARM STUDIES IN RARE DISEASE

New Approach to Reduce Clinical Development Cost and Time

SITUATION

Randomized controlled trials are used to determine the safety and efficacy of new drug treatments. Some patients are selected at random to receive the new therapy in question, while a control group receives a placebo or the current standard of care (SOC). By comparing the outcomes among patients in the treatment and control arms, the safety and efficacy of the new therapeutic can be evaluated.

However, certain ethical and practical issues can preclude the use of a multi-arm study. For example, in the trial of a treatment for end-stage disease, it would be unethical and impractical to treat a control group with a placebo or ineffective SOC. In these cases where proper control groups are not feasible, the alternative is a single-arm study, in which all patients are treated with the experimental drug. However, single-arm trials cannot always provide conclusive evidence for the safety and efficacy of a treatment compared to the current standard of care. Over 500 such single-arm trials are currently active in the United States.[1]

CHALLENGE

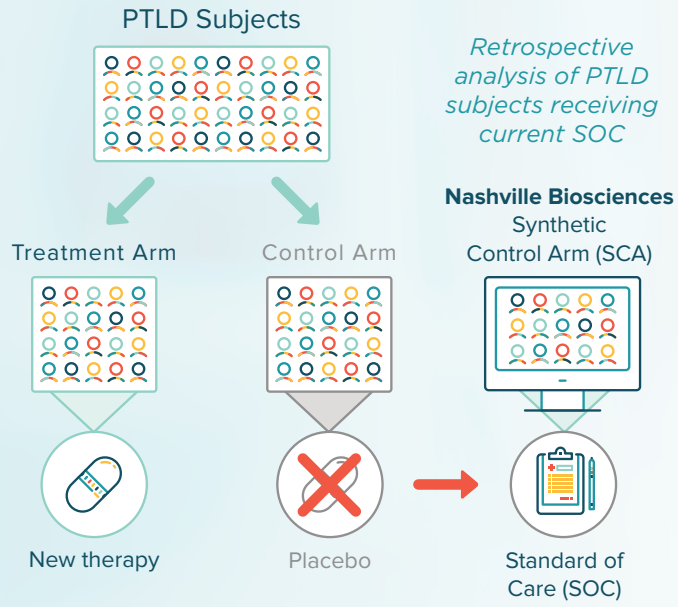
When multi-arm clinical trials are not feasible, pharmaceutical companies are faced with the challenge of maintaining the ethical integrity of clinical research while continuing to pursue evidence for the efficacy of new treatments.

In this particular case, a pharmaceutical company was conducting a Phase III single-arm clinical study on patients with an aggressive and often fatal disease, known as post-transplant lymphoproliferative disorder (PTLD). Due to small patient populations, frequent relapses following first-line therapy, and rapid progression of the disease, a true control group was not feasible. Therefore, to complement their ongoing clinical trial, the company partnered with Nashville Biosciences to conduct a retrospective study of patients with PTLD.

APPROACH

To address the limitations of the single-arm clinical trial, Nashville Biosciences leveraged a unique proprietary database of de-identified electronic medical records (EMRs), containing approximately 3.0 million patient records with an average of 10 years of longitudinal data per record. Using this database, Nashville Biosciences compiled the records of past patients treated for PTLD with the current SOC.

With the compiled EMRs, Nashville Biosciences then generated a virtual cohort of these rare disease patients, a record-based control group providing clinical data to assess response and outcomes to the current treatment standard. This virtual control group, or synthetic control arm (SCA), yielded real-world outcomes data in the absence of a true control arm. Nashville Biosciences provided data to assess disease incidence, treatment response, lab values, relevant medical history, survival status, and health resource utilization.



BENEFITS & RESULTS

Providing Critical Evidence

The SCA from Nashville Biosciences provided the partner company with detailed data on patient outcomes under the current PTLD SOC, enabling evaluation of the efficacy of the experimental therapy against the current alternative in terms of overall response rate, overall survival rate, and progression-free survival rate. For the more than 500 active single-arm trials in the United States,[1] this solution encourages optimism for the possibility of control data where it would otherwise be unavailable.

Reduced Costs & Time

Along with providing a platform for evaluating treatments without the need for a traditional control arm, the SCA approach dramatically reduces cost and trial duration. While a typical Phase III study costs $10 – $50 million and takes 1 to 4 years,[2,3] this study was performed at a far lower cost and took only three months from start to finish, including patient selection and extensive manual EMR review.

New Therapies to Market

Control data for experimental treatments provides payors the assurance that new therapies are effective and help fulfill an unmet need. The SCA study from Nashville Biosciences widens the range of treatments for which this data can be generated, while reducing trial duration and costs necessary to bring a new therapy to market. The SCA approach is expected to save years of R&D efforts, help identify subpopulations that would benefit from the new therapy, and ultimately improve R&D efficiency.

Characteristic	Prevalence in cohort of 55 PTLD subjects
Sex	37 Male (67%) / 18 Female (33%)
Race	47 White (85%) / 8 African-American (15%)
Subjects receiving surgical treatment	24 (44%)
Subjects receiving chemotherapy	40 (73%)
Subjects receiving radiation	6 (11%)
Subjects with no response to chemotherapy	8 (15%)
Subjects with relapse/recurrence after initial best response	6 (11%)

Characteristic	Average (or prevalence in cohort of 55 PTLD subjects)
Age at diagnosis	38.4 years
Length of EMR post-diagnosis	4 years
Median survival time for chemotherapy non-responders	0.37 years

1. *http://clinicaltrials.gov*
2. *Office of the Commissioner. "The Drug Development Process - Step 3: Clinical Research." U S Food and Drug Administration Home Page, Office of the Commissioner, 4 Jan. 2018, www.fda.gov/forpatients/approvals/drugs/ucm405622.htm.*
3. *Sertkaya A, Wong HH, Jessup A, Beleche T. "Key cost drivers of pharmaceutical clinical trials in the United States." Clin Trials. 2016 Apr;13(2):117-26. doi: 10.1177/1740774515625964. Epub 2016 Feb 8. PubMed PMID: 26908540. https://www.ncbi.nlm.nih.gov/pubmed/26908540.*

ABOUT NASHVILLE BIOSCIENCES

Nashville Biosciences, a wholly owned subsidiary of Vanderbilt University Medical Center (VUMC), was created to harness the Medical Center's extensive genomic and bioinformatics resources for drug and diagnostics discovery and development.

Leveraging Vanderbilt University Innovation™, Nashville Biosciences serves as a commercial interface between outside companies and the formidable research capabilities represented by BioVU®, one of the world's most comprehensive genetic databases linked to de-identified medical records with years of longitudinal clinical data.

This unique asset is one of the largest and highest quality of its kind, providing an unprecedented opportunity to guide R&D activity in biotech, pharma, diagnostics, medical devices and other life sciences applications.

Nashville Biosciences

To learn more about Nashville Biosciences or to request a private demo of our capabilities, please visit **www.nashville.bio**