



Clinical Operations In The Age Of A Pandemic

By Len Rosenberg, Ph.D., R.Ph., Leukemia & Lymphoma Society / Beat AML Master Trial

A process and technology model based on remote monitoring and faster data acquisition – ideal for clinical trials during the current coronavirus outbreak and future pandemics

“Today is the day that virtual medicine, e-learning, and telehealth take off. Major cancer centers including ours are banning professional travel. Huge opportunity for academics and patients if we can figure out how to make it work.”

- March 4, 2020 tweet by Hal Burstein, MD, cancer specialist and professor, Dana Farber/Harvard Medical School

The Leukemia & Lymphoma Society (LLS) is a patient-focused voluntary health organization dedicated to blood cancer research and patient and professional education. In 2014, LLS met with key opinion leaders to discuss the lack of progress in developing new therapeutic approaches in acute myeloid leukemia (AML) and the urgent medical need for action, as the standard of care for AML had not changed in over 40 years. As a result, LLS developed the Beat AML (BAML) Master Clinical Trial – a collaborative trial across multiple academic centers, with the objective of testing several novel targeted therapies for AML patients with different genetic mutations.

Today, AML is the most frequently diagnosed leukemia in older adults. BAML needed to change the paradigm of clinical operations to provide life-saving treatments to patients faster than biopharma companies would have done individually. The core challenge in clinical operations for acute, complex blood cancer trials is how to collect and verify key source data without requiring monitors (clinical research associates, or CRAs) to travel to the sites to source verify safety signals and efficacy response. Not only do CRAs travel to sites to monitor source data, in line with ICH E6 (R2) and good clinical practices, they also need to verify informed consent signatures, regulatory logs, drug dispensing, and pharmacy records.

Since its inception in 2016, BAML created a next-generation clinical operations model for managing complex oncology trials (running upwards of 11 protocols simultaneously at over 15 major academic institutions) with very little dependence on CRAs in the traditional on-site visit model. BAML was focused on efficiency and speed of operations, not on the coronavirus outbreak or pandemics in general. Yet, the model and technologies used by BAML are applicable for biopharma sponsors who want to adapt their clinical operations to support remote monitoring and faster acquisition of data, while preparing for another outbreak or weathering the current crisis.

Here’s how we accomplish this: First, patients need to be properly consented. A copy of the signed informed consent is uploaded to the Protocol First (P1) electronic data capture (EDC) software’s Master Trial Screening section with unredacted patient identification included. This HIPAA-compliant environment has role-based access (i.e., only site users can upload source, and only CRAs can view it) to allow confirmation of the current informed consent form (ICF) version and signatures. Once the patient qualifies for the trial and is properly categorized in terms of genetic mutations, they get assigned to the relevant sub-study treatment assignment, and another consent is signed and follows the same process.

All key electronic medical records (EMR) surrounding patient eligibility and progress are uploaded into P1 as *certified* copies and correspond to the data entry field in the tabular case report forms (CRFs). The CRA is provided with access both to the certified copies of the medical record and to the CRF page for remote monitoring. All traditional data reviews/queries are created remotely and a corresponding remote monitoring visit report is generated.

More than half the sites now use Clinical Pipe (CP), an app that connects research institutions’ electronic health record (EHR) systems with sponsor’s EDC database. A complementary software to P1’s eSource, CP automatically pipes structured data from the EMR into the corresponding CRF entry, whether to Medidata Rave for the earlier studies or to P1 EDC for the more recent ones. This eliminates the need for both source upload and manual data transcription by the study coordinators, as well as the need for source data verification by the CRA.

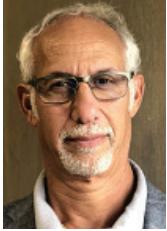
Beyond clinical and consent data, these registrational studies require training logs, delegation of authority logs, pharmacy records, etc. We have provided sites with P1 electronic study logs, which allow the sites to create key regulatory logs or to simply upload PDFs or pictures of their site-specific data. For example, most sites use Vestigo as the institutional pharmacy drug accountability system. The sites upload the data, and the CRAs can review those and all other regulatory logs remotely. This ensures ongoing audit readiness and vastly decreases the time needed on site to verify such tedious operational data.

The cost and time-saving justifications are obvious. Reducing site burden, on-site monitoring visits, and secondary data reviews and queries contributes to a successful program. We obtain key safety and efficacy data much sooner than through legacy processes and technologies. It allows us to make early decisions on cohorts in complex oncology programs. Better still, we do it (almost) all remotely, without requiring endless travel and on-site monitoring visits. Our contract research organization (CRO), Syneos Health, manages all these operational tasks.

In addition to the core source, EDC, and EHR-to-EDC technologies described above, we have also deployed innovative technologies to allow for remote, video-based protocol training using myClin. We also collaborated with Saama Technologies to create the first genomically based oncology master trial dashboard to ingest all key data feeds and display real-time laboratory (e.g., mutations, blood counts), clinical operations, and EDC analytics (risks), so as to manage the program centrally in a NASA-like mission control environment.



This morning, I read the tweet above from Dr. Hal Burstein. Will it take a global catastrophe for the inflexible, conservative, oncology clinical operations sector to adapt and adopt proven scientific and operational technologies that extend survival in front line blood cancer trials? Will next-generation clinical operations processes and technologies take off? Thanks to the specific objectives we set out on BAML, we offer a model that biopharma sponsors, CROs, and non-profit organizations can follow.



About The Author:

Len Rosenberg, Ph.D., R.Ph., is a 30+ year executive with proven experience in driving operational excellence at all levels within the pharmaceutical, biotechnology, eClinical, and CRO sectors. He brings a diverse background — which includes executive management, clinical and regulatory operations, business development, eClinical technology solutions, and new product/licensing evaluations — to optimizing the drug development cycle, from the early start-up stage to global product registration across many key therapeutic areas including CNS and oncology. Rosenberg is managing partner of eP2Consulting, Inc. and also currently serves as head of Clinical Operations at Beat AML, LLC, a division of The Leukemia & Lymphoma Society.