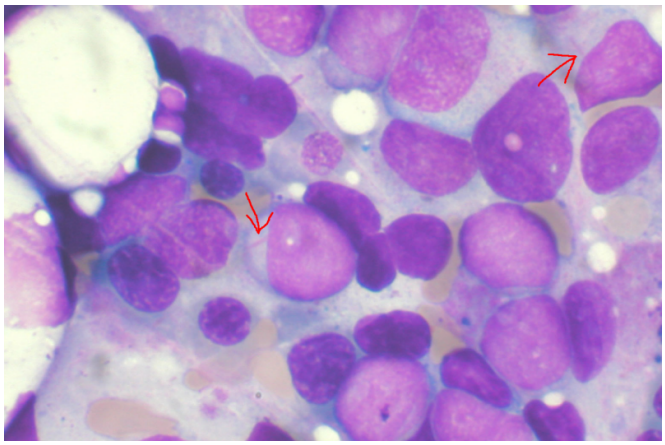
Superior outcomes for acute myeloid leukemia patients in clinical trial

27 October 2020, by Andrea Greif



Bone marrow aspirate showing acute myeloid leukemia. Several blasts have Auer rods. Credit: Wikipedia

Patients participating in The Leukemia & Lymphoma Society's (LLS) groundbreaking precision medicine Beat AML Master Clinical Trial had superior outcomes compared to acute myeloid leukemia (AML) patients who opted for standard chemotherapy treatment, according to findings published today in *Nature Medicine*.

The Beat AML trial achieved its primary endpoint by showing genomic analysis of the leukemia cells to identify AML subtypes can be completed within an unprecedented seven days, giving patients, caregivers and their doctors ample time to make a more personalized treatment decision without risking the patient's chance for survival.

In other key findings, the study demonstrated a paradigm shift in how patients diagnosed with AML should be treated, proving that using genetic information to match patients to targeted therapies leads to better survival rates than the traditional one-size-fits all treatment approach.

AML is an extremely fast-moving cancer of the marrow and blood, affecting 21,000 people in the U.S. a year, and killing 10,000. For decades patients have been given the same treatments almost immediately upon diagnosis because waiting allows the cancer cells to grow out of control. This standard of care involves either infusion of a combination of two chemotherapies, cytarabine and daunorubicin, or treatment with a so-called hypomethylating agent, a drug that unleashes signals allowing the cancer cells to die.

"The study shows that delaying treatment up to seven days is feasible and safe, and that patients who opted for the precision medicine approach experienced a lower early death rate and superior overall survival compared to patients who opted for standard of care," said John C. Byrd, MD, D. Warren Brown Chair of Leukemia Research of The Ohio State University, and one of the Beat AML leads and corresponding author of the study. "This patient-centric study shows that we can move away from chemotherapy treatment for patients who won't respond or can't withstand the harsh effects of the same chemotherapies we've been using for 40 years and match them with a treatment better suited for their individual case."

Going on the Offensive Against AML

Recognizing the urgent need to do better for AML patients, LLS launched this clinical trial in fall 2016 to test multiple novel targeted therapies at major cancer centers across the U.S., in newly diagnosed AML patients aged 60 and older. In a historic first for cancer clinical trials, LLS is the first non-profit health organization to sponsor a trial and hold the IND (Investigational New Drug) application from the U.S. Food and Drug Administration. Beat AML partnered with Foundation Medicine Inc. to employ next generation genomic sequencing to rapidly analyze the patients' cancer cells, and identify the patients' AML subtype so they can be given a targeted therapy within a safe timeframe.

"The breadth of this collaboration, with every clinician, cancer center, pharmaceutical partner and all of the many operations and technical support companies, all unified in working toward the common goal of building a new model for tackling this challenging disease, was truly inspiring," said Amy Burd, Ph.D., LLS vice president of research strategy, and first author on the paper.

Drs. Byrd and Burd were joined by Brian Druker, MD, Director, Knight Cancer Institute at Oregon Health & Science University, and Ross L. Levine, MD, Director of the Center for Hematologic Malignancies at Memorial Sloane Kettering Cancer Center, in leading a team of renowned academic researchers and other collaborators to plan, develop and launch Beat AML. To date, the trial, which is ongoing, has screened more than 1,000 patients at 16 cancer centers. The data presented in today's Nature Medicine publication represents patient enrollment during a slice of time between November 17, 2016 and January 30, 2018.

Of 487 patients with suspected AML who agreed to participate during that timeframe, 395 were found eligible for the trial. Screening and analysis was successfully completed within the seven-day timeline for 374, or 94.7 percent, of those patients. Ultimately, 224 of those patients opted to participate on one of the 11 study arms that were active during that period. The patients who didn't chose to join the study either opted for standard of care, palliative care, or an alternative clinical trial.

The median overall survival for patients in Beat AML was 12.8 months v. 3.9 months for patients opting for standard of care.

"The study is changing significantly the way we look at treating patients with AML, showing that precision medicine, giving the right treatment to the right patient at the right time, can improve short and long-term outcomes for patients with this deadly blood cancer," said Louis J. DeGennaro, Ph.D. president and CEO of LLS. "Further, Beat AML has proven to be a viable model for other cancer clinical trials to emulate."

Indeed, LLS recently launched its Beat COVID trial, leveraging rapidly the Beat AML infrastructure to quickly pivot to treat blood cancer patients who are infected with the COVID-19 virus. Studies show blood cancer patients are between 30-60% at risk of death if infected with the COVID-19 virus and Beat COVID is testing a drug called acalubrutinib (Calquence), already approved to treat several types of blood cancers. The drug shows promise in addressing deadly symptoms of COVID-19, such as inflammation of lungs and other vital organs. The trial is open to patients diagnosed with all types of blood cancers.

LLS is also planning other precision medicine trials modeled after Beat AML, including LLS PedAL, a global precision medicine trial for children with relapsed acute leukemia, on track to launch in summer 2021, and Stop MDS, a master trial for patients with myelodysplastic syndromes, a blood cancer that frequently progresses to AML.

More information: Amy Burd et al. Precision medicine treatment in acute myeloid leukemia using prospective genomic profiling: feasibility and preliminary efficacy of the Beat AML Master Trial, *Nature Medicine* (2020). DOI: 10.1038/s41591-020-1089-8

Provided by Leukemia & Lymphoma Society