

What's Next in Blood Cancer: Looking Ahead to 2023

Immunotherapy leads the way, along with promising breakthroughs for treating leukemia and multiple myeloma.

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The most important blood cancer scientific meeting, the American Society of Hematology (ASH), is held every December. This meeting, followed closely by the start of the new year, is the perfect time to reflect on progress in patient care and ongoing research, much of it supported by The Leukemia & Lymphoma Society, that is advancing cures and improving quality of life for blood cancer patients.

LLS presented its own new research at ASH, led a symposium with prominent blood cancer researchers to discuss next generation research, participated in two expert roundtables about improving equitable access to clinical trials and clinical care, and listened as hundreds of LLS-funded researchers and current and former [LLS Therapy Accelerations Program](#) partners shared their research findings.

Here are some of the highlights of ASH and some thoughts on what to expect in 2023.

Immunotherapy Will Continue to Lead the Way in Blood Cancer Care & Cures

The hot topic at this year's ASH was bispecific antibodies. These new treatments (two were FDA-approved in 2022: [teclistamab \[Tecvayli\] for multiple myeloma](#) and [mosunetuzumab \[Lunsumio\] for follicular lymphoma](#)) attach to both the surface of cancer cells and immune T-cells to bring them together and engage the T-cells to kill the cancer. While most antibody treatments latch on to a single target, bispecific antibodies bind two different targets on two different cells at the same time, expanding the potential for therapeutic options.

Clinical trials reported at ASH demonstrate efficacy and safety of other bispecifics. Here are highlights from new clinical trial results with bispecifics:

- More than 4 in 5 patients with either newly diagnosed or advanced follicular lymphoma (FL) had no detectable cancer after being treated with combination therapy that included the bispecific drug epcoritamab. In another study, 2 in 3 patients with diffuse large B-cell lymphoma (DLBCL) had no detectable cancer after treatment with an epcoritamab-containing combination. Only time will tell how long these results will last, but what we see so far is very promising. FDA is slated to decide on epcoritamab's approval by May.
- In January 2023, the FDA granted priority review status to another bispecific presented at ASH. Glofitimab induced early and durable responses in patients with advanced large B-cell lymphoma (LBCL). Twelve months after the end of treatment, 61% of patients in the study (37 of 61) had no detectable signs of their cancer.
- In early December, FDA accepted the new drug application for talquetamab. As presented at the recent ASH annual meeting, talquetamab is a bispecific antibody that binds to a distinct site on myeloma cells compared to teclistamab and engages T-cells. In heavily treated relapsed/refractory myeloma patients, the drug produced a high response rate associated with a median progression-free survival of 7.5 months.
- Adding the bispecific blinatumomab to chemotherapy keeps patients with B-lineage acute lymphoblastic leukemia in remission and extends survival time. At 43 months after initiation of therapy, survival rates jumped from 65% in those on chemo alone to 83% when the bispecific was added.
- LLS TAP partner, Affimed, preloaded a bispecific antibody, known as AFM-13, onto immune cells called natural killer (NK) cells. When infused back into patients, the bispecific antibody binds to a target known as CD30 on Hodgkin lymphoma cells. AFM-13 produced a 100% response rate in

patients with relapsed/refractory Hodgkin lymphoma.

With 12 approvals in the last five years, including four in 2022, CAR T-immunotherapy has been a life saver for some blood cancer patients. But CAR T doesn't work for everyone, it has to be administered at specialized centers, and it must be manufactured from T-cells derived from the patient, which is a time-consuming process. Data presented at ASH confirms long-term effectiveness of CAR T therapies for some patients, but also how newer generation therapies may overcome some of their limitations.

- [LLS Therapy Acceleration Program](#) (TAP) partner Caribou Biosciences' reported results for its "off-the-shelf" CAR T, which can be administered sooner than CAR T therapies that need to be tailor made for each patient. Caribou's treatment, called CB-010, led to a complete cancer response in all six patients with non-Hodgkin lymphoma in the clinical trial. Two of the patients had no sign of cancer for at least a year and one patient maintained the response for 18 months.
- Despite recent advances in treatments for chronic lymphocytic leukemia, CLL remains incurable in most patients. Researchers reported data from an early trial evaluating brexu-cel (Tecartus) in CLL (the treatment is already approved for forms of NHL). The trial was designed to test the drug's safety (no unexpected safety issues arose), but early efficacy data showed just under half of the patients (7 of 15) responded to treatment including two with a complete response (no detectable cancer). These results are especially promising, since these are patients whose cancer had stopped responding to all other treatments.

New Drug Class Produces Complete Responses in Patients With Acute Myeloid Leukemia

There were multiple new and encouraging treatment modalities reported at ASH for leukemia (and in addition, FDA approval of a [new targeted therapy](#) [Rezlidhia] in December for people whose AML carries a specific gene mutation called IDH1).

One of the most exciting new treatments modalities are menin inhibitors, which could be the next new class of drug approved to treat some forms of acute myeloid leukemia (AML). LLS supported

foundational research by Dr. Jolanta Grembecka (University of Michigan) into the role of menin that started over 15 years ago. Today, LLS supports menin inhibitor drugs being evaluated as a treatment.

In Phase 1 clinical trials, the overall response rate with two menin inhibitors, revumenib or ziftomenib, is approximately 40%-60%. In addition, 30% of people with specific AML mutations called NPM1 had complete disappearance of their leukemia and restoration of normal blood function after treatment with menin inhibitor revumenib. LLS is supporting trials for drugs that target menin, which could be available to patients within two to five years.

Menin inhibitors will be a big step forward for AML treatment, but it will likely take a combination of drugs to reach the ultimate goal—AML cure. AML in particular will require a cocktail of drugs because it is marked by many mutations that can change over time and become resistant to certain treatments. LLS is already supporting new studies to examine the basis of resistance to menin inhibitors in anticipation of identifying patients who might otherwise have excellent responses to menin inhibitors if we can develop strategies to overcome resistance when it occurs.

AML is one of LLS's priority research initiatives and we convene two master clinical trials focused on providing timely and targeted AML treatment to both children (PedAL trial) and adults (Beat AML® trial). Both trials focus on identifying the unique genetic markers on an individual patient's cancer and getting the patient into a clinical trial that works against them.

More Treatment Options Are on the Horizon for Chronic Leukocytic Leukemia

In addition to the CAR T-immunotherapy brexu-cel, there are several other new drugs in clinical testing for patients with CLL, who live with the expectation of periodic relapses, each being more difficult to treat than the last.

One of the most notable studies discussed at ASH showed that a next generation BTK inhibitor called zanubrutinib is easier to tolerate and more effective than the widely used ibrutinib in treatment of patients with relapsed or refractory CLL. These drugs block the BTK enzyme, which is essential to growth and survival of CLL and other B-cell blood cancers.

The good news here is that new therapies are evolving faster than patients are relapsing, so when they do relapse, chances are there will be a new option. Other CLL drugs in development reported at ASH include non-covalent BTK inhibitors (zanubrutinib and ibrutinib are covalent) and BTK degraders. All target BTK, but the non-covalent inhibitors and BTK degraders work through different mechanisms and thereby can overcome resistance to the covalent BTK inhibitors.

New Genetic Targets, New Breakthroughs in Multiple Myeloma Treatment

As with CLL, there has been significant improvement in the treatment of multiple myeloma, but a

cure remains elusive. Despite improved survival rates, most patients who achieve complete responses to treatment will eventually experience disease progression.

In 2021–2022 there were big steps forward in multiple myeloma treatment with approval of three immunotherapies—the bispecific antibody teclistamab and the CAR Ts, [cilta-cel](#) (Carvykti) and [ide-cel](#) (Abecma). All three drugs target BCMA, which is highly expressed on the surface of myeloma cells .

The GPRC5D protein is overexpressed in the bone marrow of myeloma patients and is a new target for immunotherapy. Two companies presented data from trials of their bispecific drug candidates targeting this protein, while a third presented early data from its CAR T-immunotherapy focused on the same genetic target. Both the J&J (talquetamab) and Roche (RG6234) bispecific drugs presented positive data from early clinical trials. The J&J drug, which is further along, was evaluated in patients who received a median of five prior therapies and led to an overall response rate of more than 70%, lasting nine months or longer. Talquetamab is under priority review at the FDA so this drug may be approved in 2023 for the treatment of relapsed/refractory myeloma.

COVID-19 in bBlood Cancer Patients

LLS presented new data from its LLS National Patient Registry at ASH, which followed the immunological response to COVID-19 mRNA vaccines in thousands of patients with blood cancer. We have observed that in many patients with blood cancer, particular those where B-cells are impaired (these cells make antibodies to the COVID-19 protein known as the spike protein), there is insufficient anti-spike antibodies produced after COVID vaccination (because the mRNA vaccines made by Moderna and Pfizer were the first available, our data has followed patients receiving these vaccines). These patients remain at risk of acquiring COVID-19 infections and having worse outcomes compared to individuals with healthy immune systems.

In addition, our new work has demonstrated that breakthrough infections occur after COVID-19 vaccinations or administration of a monoclonal antibody cocktail known as EvuSheld that were given during the post-Omicron surge. According to the latest data from CDC and newly published data from academic laboratories, the current viral strains of COVID-19 (BQ.1.1, BQ.1 XBB.1.5), which are derived from the Omicron, evade all previously FDA-emergency authorized monoclonal antibodies.

We urge all blood cancer patients to remain vigilant, get the bivalent vaccine, and report any COVID-19 infection to their physician immediately. The antiviral agent, Paxlovid, remains effective against the latest viral strains of COVID-19.

Looking Forward

LLS has been instrumental in the development of nearly every breakthrough in blood cancer since our founding. Our success drives us to do even more, work even harder, and be even more innovative for the patients and families we serve.

I say it every year and every year it's true. We've come a long way and we continue to make substantial progress.

The outlook for blood cancer patients is better than ever, but it's still nowhere near good enough. With more than \$233 million dollars currently committed to research into every type of blood cancer, you can be sure LLS is not done driving innovative research into cures and improved quality of life; providing personalized, one-on-one support to cancer patients and their families; and advocating for policy changes that accelerate the development of new cancer treatments and break down barriers to care.

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<http://beta.docker.cancerhealth.com/article/next-blood-cancer-looking-ahead-2023>