Blinatumomab: A novel, bispecific, T-cell engaging antibody

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Leukemia is a rare malignancy in adults, being the ninth most common new cancer in men (30,900 cases) and women (23,370 cases) and the sixth most common cause of death from cancer in men (14,219) and women (10,240) in 2015. In children, leukemia represents 30% of all cancers diagnosed. The lifetime probability of developing leukemia is 1.7% for men and 1.2% for women. Fortunately, death rates have declined at about 1% per year. There are four types of leukemia. Acute lymphoblastic leukemia (ALL) is the least common type of leukemia and is the focus of this article.

In 2015, the estimated number of new adult ALL cases was 6,250 (3,100 men and 3,150 women), with an estimated 1,450 deaths (800 men, 650 women). ALL accounts for approximately 75% of all leukemia cases in children, with a five-year survival rate of 89%. In terms of ALL diagnosis, there are two distinct peaks: between 4 and 10 years of age and after age 50 years. With ALL comprising approximately one third of malignancies diagnosed in children, it is generally considered a pediatric malignancy.

The median age of ALL diagnosis is 14 years, with 60% of patients diagnosed under the age of 20 years. ALL represents approximately 75% of childhood leukemias. Approximately 20% of leukemias diagnosed in adults are of the ALL subtype, with diagnosis occurring after age 45 years in 24% of patients and at age 65 or older in 11% of patients. Five-year overall survival rates are far superior in pediatric patients compared with adult patients (>80% versus <40%).

ALL originates in B- or T-lymphocyte progenitor cells and con-
Continuous proliferation of leukemic cells leading to suppression of normal hematopoiesis. The overpopulation of the leukemic clone can lead to involvement of extramedullary sites such as the liver, spleen, lymph nodes, thymus, meninges, and gonads. Several decades of research now allows ALL to be categorized by prognostically and therapeutically important subtypes and has helped identify important therapeutic targets.

In 2008, the World Health Organization classified ALL into three main subtypes: B-lymphoblastic leukemia/lymphoma (B-ALL), B-ALL with recurrent cytogenetic abnormalities, and T-lymphoblastic leukemia/lymphoma. Patients with B-ALL are often further stratified by age and the presence of specific cytogenetic abnormalities. Patients have historically been classified as pediatrics and adults, with a cutoff age of 18–21 years of age. Recently, the adolescent and young adult patient population has been a group of interest. This unique group, age 15–39 years, may receive either pediatric- or adult-based treatment protocols. The response rates for these patients are typically worse than for pediatric patients but better than the typical response rates of adult patients when more-intense pediatric regimens are used. Another major focus for treatment stratification is the presence of the Philadelphia (Ph) chromosome, t(9;22), which results in a translocation of the ABL1 gene on chromosome 9 to be a part of the BCR gene on chromosome 22. This specific abnormality is present in approximately 25% of adult patients and 2–4% of pediatric patients diagnosed with ALL. The frequency of Ph chromosome-positive ALL increases with age: 10% in patients age 15–39 years, 25% in patients age 40–49 years, and 20–40% in patients older than 50 years. Patients who test positive for the BCR-ABL translocation receive treatment with tyrosine kinase inhibitors directed toward this mutation in addition to standard therapy. This combination treatment approach has greatly improved outcomes for patients with this specific abnormality. Ph chromosome-positive patients have a complete remission (CR) rate of 83% and a 5-year overall survival rate of 25%. Patients with Ph chromosome-negative ALL have CR rates of 84–97% and 5-year overall survival rates of 23–54%. The ability of several tyrosine kinase inhibitors to target the BCR-ABL mutation in Ph chromosome-positive ALL has resulted in improved patient outcomes. New treatment options are needed for the treatment of Ph chromosome-negative ALL, as the choices for patients with relapsed or refractory disease are limited and ineffective for obtaining durable responses. The purpose of this review is to describe a new treatment option for adult patients with relapsed or refractory Ph chromosome-negative B-ALL.

**Ph chromosome-negative B-ALL**

Traditional treatment of patients with Ph chromosome-negative B-ALL takes a total of two to three years to complete and comprises several phases of treatment: induction, consolidation, and maintenance. The initial goal of treatment is to achieve CR, which is typically done by administering a complex chemotherapy regimen consisting of prednisone, vincristine, cyclophosphamide, and daunorubicin, with or without pegaspargase. CR rates typically range from 85% to 95%, with treatment-related mortality rates of 5–10%. Once CR is achieved, therapy is consolidated or intensified to maintain CR. During this step, agents used during induction may be administered as well as cytarabine, methotrexate, and mercaptopurine. Central nervous system (CNS) prophylaxis is also administered. The CNS is a potential site of leukemia relapse because systemic chemotherapy cannot readily cross the blood-brain barrier and eradicate leukemic cells that may be located there. CNS prophylaxis or treatment can be accomplished through the use of intrathecal chemotherapy, high-dose chemotherapy that can penetrate the CNS, or radiation. Once remission is achieved and intensification and consolidation are complete, therapy to maintain remission is initiated. Maintenance treatment is administered for two to three years and typically comprises mercaptopurine and weekly methotrexate, with some regimens also incorporating vincristine and prednisone. The length of maintenance therapy has been extrapolated from pediatric patients, as it has not been established in adults.

The majority of adults diagnosed with ALL will relapse (60–70%). The median overall survival after relapse is very short (4.5–6 months), with five-year overall survival rates of 7–10%. Salvage regimens typically contain elements from induction therapy and lead to CR rates of 20–30%.

In an attempt to prevent disease relapse, select patients may undergo allogeneic hematopoietic stem cell transplantation (HSCT) as a consolidation strategy. If transplantation is determined to be a viable option, patients considered to have high-risk disease typically undergo allogeneic HSCT in first remission, leading to five-year overall survival rates of 44–53%. Despite the benefits of allogeneic HSCT, this strategy may not always be used in first CR due to the unavailability of a donor as well as advanced age and comorbidities of the patient.

Despite the advances made in the diagnosis, classification, and treatment of ALL, improved therapies are needed due to the high relapse rate and ALL’s refractoriness to conventional treatment. On December 3, 2014, blinatumomab (Blincyto, Amgen) was approved via an accelerated pathway by the Food and Drug Administration. Blinatumomab (Blincyto, Amgen) was approved via an accelerated pathway by the Food and Drug Administration.

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Administration for the treatment of adult patients with Ph chromosome-negative relapsed or refractory B-cell precursor ALL.\textsuperscript{13} 

Chemistry and pharmacology

The CD19 antigen is expressed during the early stages of B-cell maturation and development and is present in nearly 95% of patients with B-cell precursor ALL, making it an attractive antigen for targeted drug therapy.\textsuperscript{14}

Blinatumomab is a novel, bispecific T-cell engaging (BiTE) antibody that targets both tumor-associated antigens CD19 (expressed on B cells) and CD3 (a receptor on T cells).\textsuperscript{15} Blinatumomab consists of two single-chain recombinant antibodies that have little distance between the two that joins CD19 and CD3 by a flexible, non-glycosylated five-amino acid non-immunogenic linker.\textsuperscript{16} Blinatumomab uses patients’ own cytotoxic T cells to kill CD19+ malignant B cells. Blinatumomab-mediated T-cell activation involves the transient proliferation of T cells and release of inflammatory cytokines.\textsuperscript{15} Blinatumomab targets CD19-expressing cells and recruits CD3 cytotoxic T cells to lyse CD19-expressing B cells,\textsuperscript{17} thus combining two antigen-binding sites: one specific for T cells and the other for CD19-expressing cells. Blinatumomab allows T cells to kill both resting and proliferating tumor cells. Blinatumomab engages patients’ endogenous T cells to attack and potentially eradicate B-cell precursor ALL blasts.\textsuperscript{14} Conventional monoclonal antibodies, which lack the dual specificity of BiTE antibodies, do not draw T cells and B-lineage ALL cells together for the same degree of highly potent tumor-cell killing.

Pharmacokinetics and pharmacodynamics

A Phase II study of blinatumomab was conducted in 21 patients receiving a four-week continuous infusion.\textsuperscript{18} After the start of each four-week continuous infusion, blinatumomab levels and lymphocyte subpopulations were measured. The levels were evaluated at 0.75, 2, 6, 12, 24, 30, and 48 hours after the start of each cycle, as well as on treatment days 7, 14, 21, and 28 and one week after the end of each treatment cycle. When blinatumomab was administered as a continuous i.v. infusion, doses as low as 0.005 mg/m\textsuperscript{2}/day eliminated the target cells in the blood, and a dose of 0.015 mg/m\textsuperscript{2}/day induced serum concentrations of 0.6 ng/mL, which remained steady throughout the duration of the infusion. In one study, the mean ± S.D. steady-state serum concentration of blinatumomab was 731 ± 163 pg/mL and was reached within 1 day.\textsuperscript{19} The steady-state serum concentration was similar with cycles 2–4. The mean ± S.D. volume of distribution was 1.61 ± 0.74 L/m\textsuperscript{2}, and the mean ± S.D. clearance of blinatumomab was 22.3 ± 5 L/day/m\textsuperscript{2}. Blinatumomab had a short mean ± S.D. elimination half-life of 1.25 ± 0.63 hours.

Within the first few hours after blinatumomab administration, there is a rapid transient decrease in T cells, followed by an accelerated increase in T cells exceeding baseline values.\textsuperscript{18} The initial fall in T cells is attributed to a redistribution phenomenon thought to be caused by an increased adhesion of T cells to the blood vessels, triggered by monovalent binding of blinatumomab to CD3. After nadir, T cells increase in number, likely due to stimulation by subsequent cytokine release. B cells rapidly decrease in less than a day, are below the limit of detection in less than two days, and remain undetectable for the duration of the blinatumomab infusion. This latter phenomenon is attributed to B-cell apoptosis. The low dose of blinatumomab needed for response (compared with conventional antibodies) is likely related to the high lytic potential of cytotoxic T cells. These T cells are activated by the engagement of only a few CD3-receptor subunits, can rapidly adopt a serial lysis mode, and can proliferate at the site of their activation. This pattern was observed in 8 of 17 evaluable patients.\textsuperscript{18} The effector memory T-cell subset exhibited the major portion of expanded cells, while both CD4 and CD8 T-cell subpopulations always exhibited an increase; however, the naive T-cell subset was basically unchanged.

Clinical efficacy

Remarkable single-agent activity of blinatumomab in adults with B-cell precursor ALL was reported in two Phase II clinical trials. One was an open-label, multicenter, single-arm trial that included 21 adults with B-cell precursor ALL in complete hematologic remission who were classified as being molecularly refractory (i.e., never having achieved minimal residual disease [MRD] negative status) or having molecular relapse (i.e., the patient becomes MRD positive after being MRD negative).\textsuperscript{18} Blinatumomab 15 µg/m\textsuperscript{2}/day was administered by continuous i.v. infusion to each patient for four weeks, followed by a two-week treatment-free interval. After one cycle of treatment, 16 (80%) of the 20 evaluable patients achieved MRD-negative status. At a median follow-up of 15 months, the probability of relapse-free survival at one year was 78%.

The other Phase II investigation was an international, multicenter, open-label, single-group trial of 189 patients with Ph chromosome-negative relapsed or refractory B-cell precursor ALL.\textsuperscript{14} Key inclusion criteria included adults with primary refractory disease after treatment induction or who had (1) relapsed within 12 months of first remission, (2) relapsed within 12 months of receiving allogeneic HSCT, or (3) not responded to or relapsed after first salvage therapy. The median
overall survival is approximately 5–9 months. Blinatumomab 28 μg/day was administered by continuous i.v. infusion via a portable pump attached to each patient for four weeks, followed by a two-week treatment-free period. The dosing schedule was completed in a stepwise approach during cycle 1, as established in the previous Phase II dose-finding study. The stepwise approach included a 9-μg/day continuous infusion administered for one week, followed by a 28-μg/day continuous infusion for the next three weeks to reduce the risk of cytokine release syndrome (CRS). Dexamethasone phosphate 10–24 mg/m²/day i.v. for up to five days was also given as a premedication to patients with more than 50% bone marrow blasts, peripheral blood blasts of ≥15,000 cells/μL, or elevated lactate dehydrogenase concentrations, suggesting rapidly progressing disease per investigator opinion. Disease status was determined by bone marrow biopsy at baseline, at the end of each cycle, and during follow-up. Dexamethasone phosphate 20 mg i.v. was administered within one hour before treatment initiation to minimize infusion reactions to blinatumomab. Patients who achieved CR or complete hematologic response within the first two cycles could receive up to three additional cycles. CR or complete hematologic remission was obtained by 81 patients (43%, 95% confidence interval [CI], 36–50%) after two cycles. Of these 81 patients, 64 (79%) obtained a CR or complete hematologic remission after the first cycle. After controlling for bone marrow blast count and lactate dehydrogenase at baseline in week 1, with dexamethasone given for CRS reduction or with dexamethasone administration before baseline bone marrow biopsy, no change in response was noted in the multivariate analysis. Of the 82 patients who had achieved a CR or complete hematologic remission, 37 (45%) remained in remission after a median follow-up time of 8.9 months (interquartile range, 4.6–11.1 months). Of the 45 remaining patients, 37 relapsed or died without documented relapse (7 patients, 6 of whom died after allogeneic HSCT; 1 patient without allogeneic HSCT died from an infection). The median relapse-free survival times were 5.9 months (95% CI, 4.8–8.3 months) for the 82 patients in CR or complete hematologic remission, 6.9 months (95% CI, 4.2–10.1 months) for patients in CR, and 5.0 months (95% CI, 1.4–6.2 months) for those in complete hematologic remission. After a median follow-up of 9.8 months, the median overall survival time was 6.1 months (95% CI, 4.2–7.5 months) for all 189 patients. This trial found that despite patients being heavily treated, a high MRD response was possible.

Despite limited pediatric experience with blinatumomab, pharmacokinetic data from the first Phase I study of blinatumomab in children indicate serum concentrations similar to those achieved in adults. Within 48 hours of receiving continuous-infusion blinatumomab, steady state concentrations were attained. The Phase I portion of that Phase I/II multicenter study was conducted to determine the optimal dose of blinatumomab in patients younger than 18 years with relapsed or refractory B-cell ALL, identifying 15 μg/m²/day i.v. as the maximum tolerated dose. CRS was the dose-limiting toxicity. In order to reduce the risk of CRS, a dose of 5 μg/m²/day i.v. for 7 days was administered, after which 15 μg/m²/day was given for the remainder of the first cycle (21 days) and all subsequent cycles. This dosing strategy was recommended for future studies in pediatric patients and has been successful in ameliorating severe CRS to date. Interestingly, it is the same dosing strategy used in adults.

Safety and tolerability

The National Cancer Institute (NCI) developed the Common Terminology Criteria for Adverse Events to aid in the recognition and grading severity of adverse events. The grade refers to the severity of the adverse event. Severity is graded as 1 (mild), 2 (moderate), 3 (severe), 4 (life threatening or disabling), or 5 (death). In the 2011 study by Topp et al., 81% of patients developed grade 3 or 4 adverse events, the most common of which was lymphopenia (33%). The majority of the adverse events were temporary, with the most common regardless of grade being pyrexia, chills, hypogammaglobulinemia, and hypokalemia. One patient had to permanently discontinue treatment during the first treatment cycle due to a grade 3 seizure that was fully reversible within one day after stopping the blinatumomab infusion. Patients received a median of 3 treatment cycles, with a total of 59.5 cycles administered in all 20 patients. No treatment-related deaths were reported.

In the 2015 study by Topp et al., 188 (99%) of 189 patients reported an adverse event of any grade. The most common adverse events regardless of grade included pyrexia (n = 113, 60%), headache (n = 65, 34%), febrile neutropenia (n = 53, 28%), peripheral edema (n = 49, 26%), nausea (n = 46, 24%), hypokalemia (n = 45, 24%), constipation (n = 39, 21%), and anemia (n = 38, 20%). Grades 3 and 4 adverse events were reported in 71 (38%) and 56 (30%) patients, respectively. The most frequently occurring grade 3 or 4 adverse events were febrile neutropenia, neutropenia, and anemia (Table 1). Fatal adverse events occurred in 23 patients (12%), with infection being the main cause. A total of 98 patients (52%) experienced neurologic events, with most being grade 1 or 2 in severity (74 [76%] of 98 patients). These events occurred mostly in cycle 1 (85 [87%] of 98 patients) and could typically be managed with dexamethasone treatment without
infusion interruption. Serious CNS toxicities included encephalopathy (3%) and ataxia (2%).

Three patients (2%) experienced grade 3 CRS.\textsuperscript{13} CR or complete hematologic remission was achieved by 2 of these patients, despite 1 having to temporarily interrupt the treatment. The third patient died from disease progression. According to the prescribing information, if a patient develops grade 3 CRS, blinatumomab should be discontinued indefinitely, if toxicity occurs at a dose of 9 µg/day or does not resolve within 7 days. The same cycle should be continued for a total of 28 days, including the days before and after the interruption; if treatment is interrupted for no more than 7 days. If treatment interruption is longer than 7 days, a new cycle should be administered. If a clinically relevant grade 3 adverse event occurs, blinatumomab should be withheld until the event is no more than a grade 1 reaction, and blinatumomab should be then resumed at 9 µg/day for 7 days, and increased to 28 µg/day if the toxicity does not recur. If the toxicity takes more than 14 days to resolve, blinatumomab should be discontinued permanently. Blinatumomab therapy should also be permanently discontinued for grade 4 CRS, if more than one seizure or other grade 4 neurologic toxicity occurs, or if any other clinically relevant grade 4 adverse event occurs.

Corticosteroids may be used to control the toxicities associated with CRS; however, their ability to block T-cell activation is concerning despite the clinical-trial analysis showing no effect on clinical benefit.\textsuperscript{14} Studies on blinatumomab-associated T-cell proliferation and immune activation may identify more-targeted strategies to control CRS.\textsuperscript{23} Interleukin (IL)-10, IL-6, and interferon-γ, the most highly elevated cytokines in patients who develop CRS, are also elevated in hemophagocytic lymphohistiocytosis (HLH), also known as macrophage activation syndrome (MAS).\textsuperscript{24} It is hypothesized that blinatumomab-associated CRS may be induced by HLH/MAS, but the degree of cytokine elevation may not correlate with CRS severity or the response to treatment. Corticosteroids are an understandable approach for the management of CRS, as some amount of cytokine release is needed for T-cell activation and efficacy. One approach to avoid or minimize the use of corticosteroids is to administer tocilizumab (an IL-6 receptor antagonist) to produce a rapid and dramatic reversal of life-threatening CRS without impairing T-cell-mediated antitumor activity.\textsuperscript{23} While blinatumomab-induced T-cell proliferation and effector function may be maintained after tocilizumab treatment, it is also conceivable that blinatumomab activity could be compromised.\textsuperscript{24} More research evaluating the safety and efficacy of potential CRS treatment options and their impact on blinatumomab efficacy is needed.

Blinatumomab has a risk evaluation and mitigation strategy (REMS) associated with it to mitigate the risk of CRS, which may be life threatening or fatal; the risk of neurologic toxicities, which may be severe, life threatening, or fatal; and the risk of preparation and administration errors associated with the use of blinatumomab.\textsuperscript{21} Amgen sent a REMS Letter for Healthcare Providers, REMS Letter for Hospital and Home Healthcare Pharmacists, and REMS Letter for Professional Societies within 30 days of the REMS approval date and will send a repeat letter every 6 months for a total of 18 months.

### Dosage and administration

In the early trials of blinatumomab, shorter infusions (over two or four hours) at doses ranging from 0.75 to 13 µg/m² i.v. were given once, twice, or thrice weekly.\textsuperscript{16} With the shorter infusions, a high percentage of patients experienced adverse events, such as neurologic events, CRS, and infections, leading to early discontinuation of these trials. In addition, shorter infusions were accompanied by an absence of objective clinical responses or robust signs of biological activity such as a sustained

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<th>Table 1. Blinatumomab-Associated Adverse Effects Occurring With a Frequency of ≥10% (n = 189)\textsuperscript{14}</th>
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<td><strong>Adverse Effect</strong></td>
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reduction of peripheral CD19+ B cells.

Due to its relatively short half-life (about two hours) and mechanism of action, blinatumomab is administered as a continuous i.v. infusion over four weeks per cycle to maintain effective concentrations in the body for maximal cell kill.25,26 Cycle 1 is dosed as a 9-µg/day continuous i.v. infusion on days 1–7 and a 28-µg/day continuous i.v. infusion on days 8–28 as a four-week continuous i.v. infusion, followed by at least two weeks of no treatment. Subsequent cycles are dosed as a 28-µg/day continuous i.v. infusion on days 1–28, followed by at least two weeks of no treatment, for up to a total of five treatment cycles.22

After a Phase I trial investigated the pharmacokinetic profile of a continuous infusion of blinatumomab, it was determined for all subsequent trials that blinatumomab should be administered via a continuous infusion for a minimum of four weeks.25 This trial included patients with non-Hodgkin's lymphoma who received a continuous infusion of blinatumomab over four to eight weeks. The trial revealed a sustained presence of blinatumomab in the serum at highly predictable levels over the entire infusion period and showed dose linearity.

Alleviation of first-dose reactions is imperative in patients receiving treatment with blinatumomab. In order to prevent these reactions, corticosteroids are given at the start of treatment.28 The patient should be premedicated with dexamethasone phosphate 20 mg (as dexamethasone sodium phosphate) i.v. one hour before the first dose of each cycle, before a dose increase, or when restarting an infusion after an interruption of four or more hours.22

By using an implanted port and minipump system, blinatumomab may be administered in the out-patient setting despite the length of the continuous infusion.22 Patients should be admitted when initiating treatment for the first cycle for nine days, in addition to the first two days of the second cycle. Due to the complexity of this therapy, healthcare providers need to comprehensively discuss the challenging administration procedures and risks of treatment with patients and caregivers.

Economic impact

Although blinatumomab has an important role in the treatment of ALL, the cost of treatment is a concern.26 Blinatumomab is predicted to cost approximately $89,000 per cycle, with patients in clinical trials receiving a median of two to three cycles.27 When considering the drug's cost, it is important to remember the preparation and coordination costs required for 28 days of continuous infusion. One study showed the median cost for an allogeneic HSCT for a patient with ALL within the first 100 days of diagnosis to be approximately $102,574 and $128,800 in the first year after diagnosis.28 Transplant costs included inpatient and outpatient costs. Inpatient costs included room charges as well as costs incurred by the pharmacy, the blood bank (including stem cell infusion), laboratory tests, radiation therapy, and miscellaneous items, which comprised the majority of expenditures in the first 100 days of treatment.

Role in therapy

Blinatumomab is approved for the treatment of adult patients with Ph chromosome-negative relapsed or refractory B-cell precursor ALL. It is a needed addition to the limited treatment options for this difficult-to-treat patient population. Blinatumomab has been added to the National Comprehensive Cancer Network (NCCN) guidelines as a treatment option for relapsed or refractory ALL.11,29 The guidelines do not list a preference for the order in which the treatment options are used; however, due to superior CR rates, there is a strong interest in using blinatumomab first in this setting.31 Clofarabine used in combination with conventional chemotherapy results in 44% CR rates in patients with relapsed or refractory ALL, with a median overall survival of 6.5 months.30 Vincristine sulfate liposomal injection has also been studied in this patient population, but the CR rate with this agent was only 20%, with a median overall survival of 20 weeks.31 Due to the efficacy of blinatumomab in Ph chromosome-negative ALL, the drug is being evaluated in Ph chromosome-positive patients who have relapsed or refractory disease and cannot tolerate tyrosine kinase inhibitors. The NCCN guidelines have included blinatumomab as a treatment option based on the lack of suitable treatments for patients with relapsed or refractory Ph chromosome-positive ALL intolerant to tyrosine kinase inhibitors before the release of clinical trial results, as Phase II studies in this population are ongoing.31 Once a patient achieves a second CR, allogeneic HSCT should be considered.

Additional questions remain regarding the best use of blinatumomab. The incorporation of blinatumomab into traditional chemotherapy regimens will produce opportunities to increase treatment efficacy but may increase healthcare costs. There is also the potential that combination therapy may not be as effective due to a decline in T cells from the chemotherapy treatment. New immunotherapy treatments are also emerging (e.g., the anti-CD22 agent inotuzumab ozogamicin, CD19-targeting chimeric antigen-receptor T cells); however, more options are needed in view of the unfavorable outcomes for relapsed or refractory ALL, including combination therapies to avoid resistance to treatment and the integration of promising compounds into first-line therapy to prevent disease relapse.
Further studies

Blinatumomab is also undergoing evaluation in studies sponsored by NCI. The Eastern Cooperative Oncology Group has opened a Phase III randomized clinical trial comparing combination chemotherapy with or without blinatumomab in patients age 35–70 years with newly diagnosed BCR-ABL-negative B-cell lineage ALL. The primary endpoint is overall survival. The study, whose primary endpoint is overall survival, began recruiting patients in December 2013; the anticipated final data collection date is June 2018.

The Phase III, open-label TOWER study is enrolling patients randomized 2:1 to blinatumomab: investigator’s choice of chemotherapy in adult patients with relapsed or refractory B-cell precursor ALL. This study began recruiting patients in December 2013, and its primary endpoint is overall survival.

NCI is also sponsoring a Phase III study that will evaluate how well blinatumomab versus investigator’s choice of chemotherapy works in treating younger patients (age 1–30 years) with relapsed B-cell ALL. The primary endpoint is disease-free survival. The study began recruiting patients in December 2014, and the final data collection date is projected to be April 2018.

Conclusion

Blinatumomab is approved as an option for Ph chromosome-negative relapsed or refractory B-cell precursor ALL and is a needed addition to the limited treatment options for this difficult-to-treat patient population. Two Phase II clinical trials resulted in impressive results when using blinatumomab as a single agent, resulting in the drug’s approval.

References


