COG AALL1731 - A Phase 3 Trial Investigating Blinatumomab (IND# 117467, NSC# 765986) in Combination with Chemotherapy in Patients with Newly Diagnosed Standard Risk or Down syndrome B-Lymphoblastic Leukemia (B-ALL) and the Treatment of Patients with Localized B-Lymphoblastic Lymphoma (B-LLy)

Status: Recruiting

Eligibility Criteria

Sex: All
Age: 365 Days to 31 Years old
This study is NOT accepting healthy volunteers

Inclusion Criteria:

• All B-ALL patients must be enrolled on APEC14B1 and consented to Eligibility Screening (Part A) prior to treatment and enrollment on AALL1731. APEC 14B1 is not a requirement for B-LLy patients. B-LLy patients may directly enroll on AALL1731.

• Age at diagnosis:

• Patients must be >= 365 days and < 10 years of age (B-ALL patients without DS).

• Patients must be >= 365 days and =< 31 years of age (B-ALL patients with DS).

• Patients must be >= 365 days and =< 31 years of age (B-LLy patients with or without DS).

• B-ALL patients without DS must have an initial white blood cell count < 50,000/uL (performed within 7 days prior to enrollment).

• B-ALL patients with DS are eligible regardless of the presenting white blood cell count (WBC) (performed within 7 days prior to enrollment).

• Patient has newly diagnosed B-cell ALL, with or without Down syndrome: > 25% blasts on a bone marrow (BM) aspirate;

• OR if a BM aspirate is not obtained or is not diagnostic of B-ALL, the diagnosis can be established by a pathologic diagnosis of B-ALL on a BM biopsy;

• OR a complete blood count (CBC) documenting the presence of at least 1,000/uL circulating leukemic cells;

• OR patient has newly diagnosed B-cell LLy Murphy stages I or II, with or without Down syndrome.

• Note: For B-LLy patients with tissue available for flow cytometry, the criterion for diagnosis should be analogous to B-ALL. For tissue processed by other means (i.e., paraffin blocks), the methodology and criteria for immunophenotypic analysis to establish the diagnosis of B-LLy defined by the submitting institution will be accepted (diagnostic biopsy for B-LLy must be performed within 14 days prior to enrollment).

• All patients and/or their parents or legal guardians must sign a written informed consent.

• All institutional, Food and Drug Administration (FDA), and National Cancer Institute (NCI) requirements for human studies must be met.

Exclusion Criteria:

• Patient must not have secondary ALL that developed after treatment of a prior malignancy with cytotoxic chemotherapy. Note: patients with Down syndrome with a prior history of transient myeloproliferative disease (TMD) are not considered to have had a prior malignancy. They would therefore be eligible whether or not the TMD was treated with cytarabine.

• With the exception of steroid pretreatment or the administration of intrathecal cytarabine, patients must not have received any prior cytotoxic chemotherapy for either the current diagnosis of B ALL or B LLy or for any cancer diagnosed prior to initiation of protocol therapy on AALL1731.

• For patients receiving steroid pretreatment, the following additional exclusion criteria apply:

• Non-DS B-ALL patients must not have received steroids for more than 24 hours in the 2 weeks prior to diagnosis without a CBC obtained within 3 days prior to initiation of the steroids.

• DS and non-DS B-LLy patients must not have received > 48 hours of oral or IV steroids within 4 weeks of diagnosis.

• Patients who have received > 72 hours of hydroxyurea within 1 week (7 days) prior to the start of systemic protocol therapy.

• B-ALL patients who do not have sufficient diagnostic bone marrow submitted for APEC14B1 diagnostic testing and who do not have a peripheral blood sample submitted containing > 1,000/uL circulating leukemia cells.

• Patient must not have acute undifferentiated leukemia (AUL).

• Non-DS B-ALL patients with central nervous system [CNS]3 leukemia (CNS status must be known prior to enrollment).

• Note: DS patients with CNS3 disease are eligible but will be assigned to the DS-High B-ALL arm. CNS status must be determined based on a sample obtained prior to administration of any systemic or intrathecal chemotherapy, except for steroid pretreatment.

• Non-DS B-ALL patients with testicular leukemia. (Note: DS patients with testicular disease are eligible but will be assigned to the DS-High B-ALL arm).

• For LLy patients, the following additional exclusion criteria apply:

• T-Lymphoblastic Lymphoma.

• Morphologically unclassifiable lymphoma.

• Absence of both B-cell and T-cell phenotype markers in a case submitted as lymphoblastic lymphoma.

• CNS positive disease or testicular involvement.

• M2 (5%

•25% blasts) or M3 (> 25% blasts) marrow.

• Patients with known Charcot-Marie-Tooth disease.

• Patients with known MYC translocation associated with mature (Burkitt) B-cell ALL, regardless of blast immunophenotype.

• Patients requiring radiation at diagnosis.

• Female patients who are pregnant since fetal toxicities and teratogenic effects have been noted for several of the study drugs. A pregnancy test is required for female patients of childbearing potential.

• Lactating females who plan to breastfeed their infants.

• Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of their study participation.

Conditions & Interventions

Interventions:
Drug: Asparaginase Erwinia chrysanthemi, Biological: Blinatumomab, Drug: Cyclophosphamide, Drug: Cytarabine, Drug: Dexamethasone, Drug: Doxorubicin Hydrochloride, Drug: Leucovorin Calcium, Drug: Mercaptopurine, Drug: Mercaptopurine Oral Suspension, Drug: Methotrexate, Drug: Pegaspargase, Drug: Prednisolone, Drug: Prednisone, Radiation: Radiation Therapy, Radiation: Radiation Therapy, Drug: Thioguanine, Drug: Vincristine Sulfate
Conditions:
B Acute Lymphoblastic Leukemia, B Lymphoblastic Lymphoma, Down Syndrome

More Information

Description: This phase III trial studies how well blinatumomab works in combination with chemotherapy in treating patients (365 Days to 31 Years) with newly diagnosed, standard risk B-lymphoblastic leukemia or B-lymphoblastic lymphoma with or without Down syndrome. Monoclonal antibodies, such as blinatumomab, may induce changes in body's immune system and may interfere with the ability of cancer cells to grow and spread. Drugs used in chemotherapy, such as vincristine, dexamethasone, prednisone, prednisolone,

pegaspargase, methotrexate, cytarabine, mercaptopurine, doxorubicin, cyclophosphamide, and thioguanine, work in different ways to stop the growth of cancer cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. Leucovorin decreases the toxic effects of methotrexate. Giving monoclonal antibody therapy with chemotherapy may kill more cancer cells. Giving blinatumomab and combination chemotherapy may work better then combination chemotherapy alone in treating patients with B-ALL. This trial also assigns patients into different chemotherapy treatment regimens based on risk (the chance of cancer returning after treatment). Treating patients with chemotherapy based on risk may help doctors decide which patients can best benefit from which chemotherapy treatment regimens.

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