Study of Inotuzumab Ozogamicin, Venetoclax, and Dexamethasone for Relapsed B-cell ALL

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 1 year to 39 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

Diagnosis:

- Patients must have relapsed B-ALL > 5 % bone marrow blasts with or without extramedullary disease.

- At least 20% of leukemic blasts must demonstrate surface expression of CD22 at the time of relapse by flow cytometry of a bone marrow aspirate. In the case of an inadequate aspirate sample (dry tap) or if bone marrow aspirate is unable to be obtained due to patient clinical status, then flow cytometry of peripheral blood specimens may be substituted if the patient has > 1,000/µL circulating blasts. Alternatively, CD22 expression may be documented by immunohistochemistry of a relapse bone marrow biopsy specimen.
- Patients with one of the following:
    - 2nd or greater relapse OR first relapse less than 24 months from diagnosis OR first or greater relapse in patients over 18.
    - Primary refractory disease: defined as > 1% bone marrow blasts by flow MRD after at least 2 courses of frontline chemotherapy. Patients who receive 2 courses of chemotherapy and 1 course of blinatumomab are also eligible, but no further treatment attempts beyond that are permitted.
    - Any relapse after HSCT or CAR-T therapy.
- Patients with Ph+ ALL must have had at least two prior therapy attempts and failed all available tyrosine kinase inhibitors.

Prior Therapy:

- Cytotoxic chemotherapy:

• At least 14 days must have elapsed from the completion of systemic cytotoxic therapy that is known to be myelosuppressive with the exception of hydroxyurea for cytoreduction OR conventional maintenance chemotherapy (i.e., corticosteroids, vincristine, 6MP, and/or oral methotrexate) for patient who relapse while on maintenance therapy OR lumbar puncture with intrathecal chemotherapy. Corticosteroids, vincristine, 6MP, and/or oral methotrexate must be discontinued at least 24 hours prior to the start of protocol therapy. If corticosteroids were used to modify immune adverse events of prior therapy rather than as chemotherapy, at least 14 days must have elapsed since the last dose.

Systemic corticosteroids may be administered for cytoreduction up to 24 hours prior to the start of protocol therapy. For all patients, corticosteroids may be administered as a premedication for inotuzumab ozogamicin and as treatment for allergic reactions or for physiologic replacement/stress dosing of hydrocortisone for documented adrenal insufficiency.

At least seven days must have elapsed from the administration of anti-cancer agents not known to be myelosuppressive.

- Anti-cancer agents that are antibodies

• At least 21 days must have elapsed from infusion of last dose of antibody. There is an exception for blinatumomab infusions, for which patients must have been off for at least 3 days.
* Radiation therapy

• At least 14 days must have elapsed since local palliative radiotherapy. At least 3 months must have elapsed if patient received cranial or craniospinal radiotherapy, if more than 50% of the pelvis was irradiated, or if total body irradiation was received. If other substantial bone marrow irradiation was given, at least 6 weeks must have elapsed.
* Hematopoietic stem cell transplant

• At least 90 days must have elapsed since stem cell transplant and at least 30 days from donor lymphocyte infusion. Patients must have had no more than one previous HSCT and currently have no evidence of active graft vs. host disease and must be off all immunosuppressive medications for at least 28 days.
* Chimeric antigen receptor T-cell therapy

• At least 30 days must have elapsed from the last CAR-T cell infusion. Patients may have previously received CD19 or CD22 directed CAR-T cell therapy but must still have CD22 expression on at least 20% of leukemic blasts.
* Prior Inotuzumab ozogamicin Patients with prior InO exposure must have received no more than 2.1 mg/m2 of prior InO and be at least 90 days from last dose.
* Prior Venetoclax exposure • Patients with prior venetoclax exposure are eligible provided they are at least 30 days from last dose.

Age:

- Patients must be ≥ 1 year and ≤ 39.99 years of age at enrollment.

Performance status:

- Karnofsky ≥ 50% for patients > 16 years of age and Lansky ≥ 50 for patients ≤ 16 years of age. Patients who are unable to walk because of paralysis, but who are up in a wheelchair, will be considered ambulatory for the purpose of assessing the performance score.

Organ function requirements:

- Adequate Renal Function Defined As:

• An estimated GFR of 50 mL/min/1.73m2 as determined by the Levey formula (see appendix C), cystatin C, or radioisotope determination.
* Adequate Liver Function Defined As:

- Direct bilirubin ≤ 1.5 x upper limit of normal (ULN) for age.
- SGPT (ALT) < 2.5 x the age-appropriate upper limit of normal (ULN) per local lab (unless elevation is related to leukemia involvement).
    - Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

Exclusion Criteria:

- Patients with any prior history of SOS irrespective of severity.
- Patients with isolated CNS, testicular, or any other isolated extramedullary site of relapse.
- Patients with CNS3 disease at time of enrollment regardless of marrow involvement.

Concomitant Medications:

- Investigational drugs: patients who are currently receiving another investigational drug.
- Anti-cancer agents: Patients who are currently receiving or plan to receive other anti-cancer agents (except hydroxyurea, which may be continued until 24 hours prior to start of protocol therapy, and intrathecal chemotherapy).
- Anti-GVHD or agents to prevent organ rejection post-transplant. Patients who are receiving cyclosporine, tacrolimus, or other agents to prevent either graft vs host disease post bone marrow transplant or organ rejection post-transplant are not eligible for this trial. At least 3 half-lives must have relapsed after the last dose of GVHD or anti-rejection medications.
- Patients > 10 kg AND > 24months may receive azole antifungals (See altered venetoclax dosing provided for patients on azoles).

Infection:

- Patients with known HIV, hepatitis B or C infections. Testing to prove negative status is not required for enrollment unless it is deemed necessary for usual medical care of the patient.
- Patients who have an active uncontrolled infection defined as:

    - Positive bacterial blood culture within 48 hours of study enrollment.
    - Fever above 38.2℃ within 48 hours of study enrollment with documented infection Fever that is determined to be due to tumor burden is allowed if patients have documented negative blood cultures for at least 48 hours prior to enrollment and no concurrent signs or symptoms of active infection or hemodynamic instability.
    - A positive fungal culture within 30 days of study enrollment or active therapy for presumed invasive fungal infection.
    - Patients may be receiving IV or oral antibiotics to complete a course of therapy for a prior documented infection as long as cultures have been negative for at least 48 hours and signs or symptoms of active infection have resolved. For patients with C. difficile diarrhea, at least 72 hours of antibacterial therapy must have elapsed, and stools must have normalized to baseline.
    - Active viral or protozoal infection requiring IV treatment.
- Patients known to have one of the following concomitant genetic syndromes: Blood syndrome, ataxia-telangiectasia, Fanconi anemia, Kostmann syndrome, Shwachmann-Diamond syndrome, or any other known bone marrow failure syndrome.

Pregnancy and Breastfeeding:

- There have been no human studies of inotuzumab ozogamicin or venetoclax in pregnant women. Based on safety studies, both agents have the potential to impair human male and female fertility to adversely affect human embryo-fetal development. Women of childbearing potential should be advised to avoid becoming pregnant while receiving inotuzumab ozogamicin and venetoclax. There is no known information regarding the presence of inotuzumab ozogamicin or venetoclax in human milk, the effects on the breast-fed infant, or the effect on milk production. Women should not breast-feed during treatment with inotuzumab ozogamicin or venetoclax and for at least 2 months after the final dose. Female patients of childbearing potential are not eligible unless a negative pregnancy test result has been obtained within 7 days prior to enrollment.
- Female patients who are sexually active and of reproductive potential are not eligible unless they agree to use an effective contraceptive method for the duration of their study participation and for 8 months after the last dose of inotuzumab ozogamicin or venetoclax.
- Men with female partners of childbearing potential should use effective contraception during treatment with inotuzumab ozogamicin and venetoclax and for at least 5 months after the last dose of inotuzumab ozogamicin and venetoclax.
- Lactating females are not eligible unless they agree not to breastfeed their infants.

    - Patients who have not recovered from adverse events due to prior anti-cancer therapy (i.e., have residual toxicities > Grade 2) with the exception of alopecia.
    - History of allergic reactions attributed to compounds of similar chemical or biologic composition to venetoclax or inotuzumab ozogamicin.

Conditions & Interventions

Interventions:
DRUG: Inotuzumab Ozogamicin, Venetoclax, and Dexamethasone
Conditions:
B-cell Acute Lymphoblastic Leukemia
Keywords:
Relapsed, B-ALL, B-cell Acute Lymphoblastic Leukemia

More Information

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Description:
The goal of this clinical trial is to learn if the combination of drugs Inotuzumab Ozogamicin, Venetoclax, and Dexamethasone (IoVeX) are safe to treat relapsed B-cell Acute Lymphoblastic Leukemia (B-ALL) in pediatric and adult patients. It will also learn if these drugs are well tolerated. The main questions it aims to answer are: Is the drug combination of Inotuzumab Ozogamicin, Venetoclax, and Dexamethasone (IoVeX) safe when given to patients? What medical problems do patients taking IoVeX experience? Participants will: Receive this combination of drugs for 1 cycle which is 28 days at various timepoints. If participants tolerate cycle 1 they will be eligible to continue to cycle 2 which is also 28 days. Have checkups and tests at the beginning of the study and throughout the course of each cycle.

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