Purpose

Background:

Moxetumomab pasudotox is an experimental non-chemotherapy cancer treatment drug. It targets CD22, a molecule on the surface of essentially all hairy cell leukemia cells. Moxetumomab pasudotox binds to CD22, goes into the cell, and releases a toxin which kills the cell. In a phase I trial it had activity in relapsed/refractory hairy cell leukemia with safety profile supporting further clinical study (http://ncbi.nlm.nih.gov/pubmed/22355053). This is a phase III multicenter trial designed to confirm these results.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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</thead>
<tbody>
<tr>
<td>Leukemia, Hairy Cell</td>
<td>Drug: <strong>moxetumomab pasudotox</strong></td>
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<tr>
<td></td>
<td>Drug: IV Bag Protectant for <strong>Moxetumomab pasudotox</strong></td>
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Study Type: Interventional
Study Design: Endpoint Classification: Efficacy Study
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Pivotal Multicenter Trial of **Moxetumomab Pasudotox in Relapsed/Refractory Hairy Cell Leukemia**

Further study details as provided by MedImmune LLC:

Primary Outcome Measures:
- Rate of CR in patients treated with study drug [Time Frame: Every 4 weeks] [Designated as safety issue: No]

Secondary Outcome Measures:
- Overall response rate [Time Frame: every 4 weeks.] [Designated as safety issue: No]
- Relapse free survival [Time Frame: Once patients have a Complete Response (CR), they will be followed with monthly blood work for 6 months then every 3 months for 2 years, then yearly thereafter. Bone marrow examinations at 6 months.] [Designated as safety issue: No]
Progression free survival [Time Frame: Once patients have a Complete Response (CR), they will be followed with monthly blood work for 6 months then every 3 months for 2 years, then yearly thereafter. Bone marrow examinations at 6 months.]
[Designated as safety issue: No]

Time to Response [Time Frame: Duration of Study] [Designated as safety issue: No]
TTR will be measured from start of administration to the first documentation of response (CR or PR)

Safety [Time Frame: 1st Administration through 30 Days after Last Dose] [Designated as safety issue: Yes]
Occurrence of AEs, abnormal laboratory values, and SAEs reported from 1st administration of moxetumomab pasudotox through 30 days after last dose

Pharmacokinetic [Time Frame: Duration of Treatment] [Designated as safety issue: Yes]

Immunogenic Potential [Time Frame: Duration of Treatment] [Designated as safety issue: Yes]

Estimated Enrollment: 77
Study Start Date: April 2013
Estimated Study Completion Date: May 2017
Estimated Primary Completion Date: May 2017 (Final data collection date for primary outcome measure)

<table>
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<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental: Arm A</td>
<td>Drug: moxetumomab pasudotox Drug: IV Bag Protectant for moxetumomab pasudotox</td>
</tr>
</tbody>
</table>

Detailed Description:
Background:
- Hairy cell leukemia is an indolent B-cell leukemia comprising 2% of all leukemias, or approximately 900 of the 44,000 new cases of leukemia/year in the US
- Over the last two decades, immunotoxin research has accumulated to support a role for CD22-targeted therapy in the treatment of HCL
- Moxetumomab pasudotox is a recombinant immunotoxin containing an Fv fragment of an anti-CD22 monoclonal antibody and truncated Pseudomonas exotoxin.
- Moxetumomab pasudotox has demonstrated a high complete response (CR) rate in patients with chemoresistant hairy cell leukemia (HCL) and has shown activity in pediatric acute lymphoblastic leukemia as well.
- Modification of the structure of moxetumomab pasudotox has greatly improved binding and cytotoxicity toward CD22 expressing malignant cells compared to the precursor molecule. Preclinical and clinical studies have demonstrated that this increase in binding affinity results in improved antitumor activity and tolerability
- Currently there are no approved agents with significant efficacy for HCL patients after failure of standard therapy

Design:
- This is a multicenter, single-arm study of moxetumomab pasudotox in patients with relapsed/refractory hairy cell leukemia.
- 77 patients will be enrolled to receive moxetumomab pasudotox IV on days 1, 3 and 5 of each 28 day cycle for a maximum of 6 cycles or until disease progression, unacceptable toxicity, initiation of alternate therapy or documented CR.
- If less than or equal to 2 of the first 25 patients do not achieve durable CR, no additional patients will be accrued.
- The overall IRB accrual ceiling is currently set at 80 to allow for a small number of patients that cannot be assessed for response.

Eligibility:
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria:
- INCLUSION CRITERIA:
  - Patients must have histologically confirmed hairy cell leukemia or hairy cell leukemia variant with a need for therapy
  - Patients must be Pseudomonas-immunotoxin naive
  - Patients must have had at least 2 prior purine analogs, or at least 1 course of purine analog and 1 of either rituximab or BRAF inhibitor.
  - Men or women age greater than or equal to 18 years.
  - ECOG performance status less than or equal to 2.
Patients must have adequate organ function

EXCLUSION CRITERIA

- Patients who have had chemotherapy, immunotherapy or radiotherapy within 4 weeks prior to entering the study.
- Patients who are receiving any other investigational agents.
- Patients who have known brain metastases should be excluded from this clinical trial.
- Patients with clinically significant ophthalmologic findings during screening.
- Pregnant or breastfeeding females.
- Positive for Hepatitis B core antibody surface antigen unless the patient is on Lamivudine or Entecavir and Hepatitis B Viral DNA load is less than 2000 IU/mL.
- Lymph nodes greater than 4cm or prior splenectomy.
- Active second malignancy requiring treatment other than minor resection of indolent cancers like basal cell and squamous skin cancers.
- HIV-positive patients unless taking appropriate anti-HIV medications with a CD4 count of greater than 200.
- History of allogeic bone marrow transplant.
- Patients with history of both thromboembolism and known congenital hypercoagulable conditions.
- Uncontrolled pulmonary infection, pulmonary edema.
- Adequate oxygen saturation.
- Radioimmunotherapy within 2 years prior to enrollment in study.
- Adequate hematologic function.
- Adequate lung function.
- Patients with history of thrombotic microangiopathy or TTP-HUS.
- Patients with QTc interval (Federica) elevation > 500 msec based on at least 2 separate 12-lead ECGs.
- Patient on high dose estrogen.
- Patients with clinical evidence of disseminated intravascular coagulation.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01829711

Contacts

Contact: AstraZeneca Clinical Study Information Center 1-877-240-9479 information.center@astrazeneca.com

Show 52 Study Locations

Sponsors and Collaborators

MedImmune LLC

Investigators

Study Director: MedImmune LLC MedImmune LLC

More Information

Additional Information:

NIH Clinical Center Detailed Web Page

Publications:


