A Phase I Trial Of The Humanized Anti-GD2 Antibody In Children And Adolescents With Neuroblastoma, Osteosarcoma, Ewing Sarcoma and Melanoma

ClinicalTrials.gov Identifier: NCT00743496

Recruitment Status : Completed
First Posted : August 28, 2008
Last Update Posted : August 17, 2017

Sponsor:
St. Jude Children's Research Hospital

Collaborators:
Evan T.J. Dunbar Neuroblastoma Foundation
Duke University
University of Wisconsin, Madison
University Children's Hospital Tuebingen
Children's Hospital Los Angeles

Information provided by (Responsible Party):
St. Jude Children's Research Hospital

Study Description

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Brief Summary:

Relapsed and/or refractory neuroblastoma, osteosarcoma, Ewing sarcoma and melanoma are considered difficult to treat and cure. For this study we are testing the use of a new experimental (investigational) antibody called hu14.18K322A. GD2 is expressed on the surface of most of these tumor types.

Two schedules of hu14.18K322A antibody will be evaluated in this study, (1) daily for four consecutive days schedule every 28 days and (2) once weekly for 4 weeks schedule every 28 days. Approximately 25-40 participants will be required to define the maximum tolerated dose for each schedule. Participants will continue on treatment for a maximum of 4 to 8 courses or until one or more of the criteria for off-treatment are met.

Condition or disease	Intervention/treatment	Phase

Neuroblastoma Melanoma Osteosarcoma Ewing Sarcoma	Biological: Anti-GD2 antibody	Phase 1

Detailed Description:

SJGD2 is a Phase I dose finding study. The primary purpose of this phase I study is to determine the maximum tolerated dose (MTD) and dose-limiting toxicity of the humanized monoclonal anti-GD2 antibody, hu14.18K322A, in research participants with refractory or relapsed neuroblastoma or melanoma (Parts A and B) or osteosarcoma or Ewing sarcoma (Part C).

Initially, in Part A, one research participant will be treated at the lowest dose level of hu14.18K322A antibody [2 mg/m^2 daily for 4 consecutive days every 28 days (1 course)], and if no toxicity is observed then the next participant will be treated at the next dose level. This is continued until the first instance of biological activity (in the form of grade 2 side effects) is observed and from that point on a traditional phase I study design will be followed. A maximum of 4 courses may be given.

Part B: Hu14.18K322A antibody will be administered intravenously (IV) at a starting dose of 50 mg/m^2/dose weekly for 4 doses per course. One course is considered 28 days. A maximum of 8 courses may be given.

Part C: Hu14.18K322A antibody will be administered to 6 patients each with refractory/recurrent osteosarcoma at a maximum tolerated dose (MTD) of 60 mg/m^2 daily for 4 consecutive days every 28 days (Part C1). A cohort of patients with refractory/recurrent osteosarcoma or Ewing sarcoma will also be administered hu14.18K322A antibody at starting dose of 40 mg/m^2/dose weekly for 4 doses per course (Part C2). Participants will continue on treatment for a maximum of 8 courses.

Secondary objectives include:

1. Estimate the response rate, within the confines of a phase I study, to the humanized anti-GD2 antibody, hu14.18K322A.
2. Evaluate the pharmacokinetics of hu14.18K322A.
3. Examine whether or not human anti-human antibodies (HAHA) develop in participants receiving hu14.18K322A.
4. Assess the tolerability of the hu14.18K322A at the MTD of the daily x4 and the weekly dosing in patients with refractory or recurrent osteosarcoma.

Study Design

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Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	50 participants
Allocation:	N/A
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase I Trial Of The Humanized Anti-GD2 Antibody (HU14.18K322A) In Children And Adolescents With Neuroblastoma, Osteosarcoma, Ewing Sarcoma and Melanoma
Actual Study Start Date :	October 8, 2008
Actual Primary Completion Date :	April 1, 2014
Actual Study Completion Date :	April 18, 2014

Resource links provided by the National Library of Medicine

MedlinePlus Genetics related topics: Ewing sarcoma Neuroblastoma Melanoma

MedlinePlus related topics: Melanoma Neuroblastoma Soft Tissue Sarcoma

Drug Information available for: Globulin, Immune

Genetic and Rare Diseases Information Center resources: Soft Tissue Sarcoma Osteosarcoma Neuroblastoma Ewing Sarcoma Neuroendocrine Tumor Neuroepithelioma

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Group 1 Participants who consent to the study will receive Anti-GD2 antibody.	Biological: Anti-GD2 antibody Anti-GD2 antibody

Outcome Measures

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Primary Outcome Measures :

1. Determine maximum tolerated dose and dose-limiting toxicity of the humanized monoclonal anti-GD2 antibody, hu14.18K322A, in research participants with neuroblastoma, osteosarcoma, Ewing sarcoma and melanoma. [Time Frame: within 12 months of the start of therapy]

Eligibility Criteria

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Information from the National Library of Medicine

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, Learn About Clinical Studies.

Ages Eligible for Study:	up to 21 Years (Child, Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Diagnosis:
  - Part A: Recurrent or refractory neuroblastoma or melanoma.
  - Part B: Recurrent or refractory neuroblastoma or melanoma.
  - Part C: Recurrent or refractory osteosarcoma and Ewing sarcoma.
- Age: ≤ 21 years of age at the time of enrollment (i.e. participants are eligible until they reach their 22nd birthday).
- Does not have a clinically significant neurologic deficit or objective peripheral neuropathy (greater than or equal to grade 2). Peripheral (sensory or motor) neuropathy related to limb sparing procedure or amputation is allowed.
- Life expectancy: at least 8 weeks.
- Organ Function: Must have adequate organ and marrow function
- Performance status: Karnofsky ≥ 50 for > 10 years of age; Lansky ≥ 50 for children < 10 years of age.
- Prior Therapy: Patient must have fully recovered from the acute toxic effects of all prior therapy prior to enrolling on study.
  - Myelosuppressive Chemotherapy: Must not have received myelosuppressive therapy within 2 weeks prior to study entry (4 weeks if nitrosurea).
  - Biologic (anti-neoplastic agent): At least 7 days since the completion of therapy with biologic agent, including retinoic acid. Participants receiving IVIG are eligible; however, participant must not receive IVIG during the 4 days of antibody infusion.

- Radiation therapy: At least 2 weeks since prior local radiation therapy at the time of study entry.
- Growth factors: Must not have received hematopoietic growth factors (G-CSF, GM-CSF) for at least 1 week prior to study entry.
- Investigational agent: Must not have received investigational agent within 14 days of study entry.
- Immune therapy: Must not have received immunosuppressive (including glucocorticoids), immunostimulatory or any immunomodulatory treatment within 2 weeks of study entry. Steroid containing inhalers, steroid replacement for adrenal insufficiency and steroid premedication for prevention of transfusion or imaging contrast agent-related allergic reaction will be permitted.

- Patients may have had prior CNS metastasis providing: CNS disease has been previously treated and CNS disease has been clinically stable for 4 weeks prior to study entry (assessment must be made by CT or MRI).
- Written informed consent following institutional and federal guidelines.

Exclusion Criteria:

- Prior monoclonal antibody: Participants having received in vivo monoclonal antibodies for biologic therapy or for tumor imaging are eligible provided they did not experience a severe allergic reaction with the antibody.
- Pregnancy or Breast Feeding: Study participants who are pregnant are not eligible for this study. Pregnancy tests must be obtained in girls who are > 10 years of age or post-menarchal within 7 days prior to study enrollment. Males or females of reproductive potential may not participate unless they have agreed to use an effective contraceptive method during participation in the trial. Breast feeding should be discontinued if a mother wishes to participate in this study.
- Allergy: known hypersensitivity to other recombinant human antibodies.
- An uncontrolled infection.

Contacts and Locations

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Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): NCT00743496

Locations

United States, Tennessee

St. Jude Children's Research Hospital
Memphis, Tennessee, United States, 38105

Sponsors and Collaborators

St. Jude Children's Research Hospital

Evan T.J. Dunbar Neuroblastoma Foundation

Duke University

University of Wisconsin, Madison

University Children's Hospital Tuebingen

Children's Hospital Los Angeles

Investigators

Principal Investigator: Michael Bishop, MD St. Jude Children's Research Hospital

More Information

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Additional Information:

St. Jude Children's Research Hospital

Clinical Trials Open at St. Jude

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Navid F, Sondel PM, Barfield R, Shulkin BL, Kaufman RA, Allay JA, Gan J, Hutson P, Seo S, Kim K, Goldberg J, Hank JA, Billups CA, Wu J, Furman WL, McGregor LM, Otto M, Gillies SD, Handgretinger R, Santana VM. Phase I trial of a novel anti-GD2 monoclonal antibody, Hu14.18K322A, designed to decrease toxicity in children with refractory or recurrent neuroblastoma. J Clin Oncol. 2014 May 10;32(14):1445-52. doi: 10.1200/JCO.2013.50.4423. Epub 2014 Apr 7.

Responsible Party:	St. Jude Children's Research Hospital
ClinicalTrials.gov Identifier:	NCT00743496 History of Changes
Other Study ID Numbers:	SJGD2 ED FDN (Other Identifier: Evan Dunbar Neuroblastoma Foundation) NCI-2011-01150 (Registry Identifier: NCI Clinical Trial Registration Program)
First Posted:	August 28, 2008 Key Record Dates
Last Update Posted:	August 17, 2017
Last Verified:	August 2017

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Additional relevant MeSH terms:

Melanoma	Nevi and Melanomas
Sarcoma	Neoplasms, Connective and Soft Tissue
Neuroblastoma	Neuroectodermal Tumors, Primitive, Peripheral
Osteosarcoma	Neuroectodermal Tumors, Primitive
Sarcoma, Ewing	Neoplasms, Neuroepithelial
Neuroendocrine Tumors	Neoplasms, Glandular and Epithelial
Neuroectodermal Tumors	Neoplasms, Bone Tissue
Neoplasms, Germ Cell and Embryonal	Neoplasms, Connective Tissue
Neoplasms by Histologic Type	Antibodies
Neoplasms	Immunologic Factors
Neoplasms, Nerve Tissue	Physiological Effects of Drugs

Key Record Dates

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Brief Title:	A Phase I Trial Of The Humanized Anti-GD2 Antibody In Children And Adolescents With Neuroblastoma, Osteosarcoma, Ewing Sarcoma and Melanoma
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