Long Term Continuous Infusion ch14.18/CHO Plus s.c. Aldesleukin (IL-2) (LTI)

The recruitment status of this study is unknown because the information has not been verified recently.

Verified October 2012 by St. Anna Kinderkrebsforschung.
Recruitment status was: Recruiting

Sponsor:
St. Anna Kinderkrebsforschung

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Information provided by (Responsible Party):
St. Anna Kinderkrebsforschung

ClinicalTrials.gov Identifier:
NCT01701479

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History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

The main aim of this clinical trial is to find a way of giving ch14.18/CHO, in combination with subcutaneous aldesleukin (IL-2) and oral isotretinoin (13-cis-RA), to children and young people with primary refractory or relapsed neuroblastoma without intravenous morphine.

Condition	Intervention	Phase
Neuroblastoma	Drug: ch14.18/CHO Drug: Aldesleukin Drug: Isotretinoin	Phase 1 Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Phase I/II Dose Schedule Finding Study of ch14.18/CHO Continuous Infusion Combined With Subcutaneous Aldesleukin (IL-2) in Patients With Primary Refractory or Relapsed Neuroblastoma

Resource links provided by NLM:

Genetics Home Reference related topics: neuroblastoma

MedlinePlus related topics: Neuroblastoma

Drug Information available for: Isotretinoin Aldesleukin

Genetic and Rare Diseases Information Center resources: Neuroblastoma Neuroepithelioma

U.S. FDA Resources

Further study details as provided by St. Anna Kinderkrebsforschung:

Primary Outcome Measures:

- Efficacy endpoint [Time Frame: day 15 of first cycle] [Designated as safety issue: No]

  On day 15 of the first cycle in ≥ 80% of patients:

  a. an increase of 500% and/or an absolute minimum increase to ≥100 cells/mcLof the CD16/CD56 positive activated NK cells, AND
  b. a measurable ch14.18/CHO level of at least 1 µg/ml.

- Pain-toxicity endpoint [Time Frame: Day 5 of ch14.18/CHO infusion cycle 1] [Designated as safety issue: Yes]

  i.v. morphine free ch14.18/CHO infusion schedule after the first 5 days during the first cycle in >= 80% of patients

Secondary Outcome Measures:

- ADCC and activated NK cell concentrations [Designated as safety issue: No]

  ADCC and activated NK cell concentrations above baseline levels in ≥ 80% of patients.

- Soluble IL-2 receptor and CDC [Designated as safety issue: No]

  Appearance of soluble IL-2 receptor and CDC.

- HAMA and HACA [Designated as safety issue: No]

  Detection of anti-idiotype response by appearance of HAMA and HACA.

- Absolute lymphocyte count [Designated as safety issue: No]

  Increase of absolute lymphocyte counts by 50% over baseline.

- Absolute NK cell numbers [Designated as safety issue: No]

  Increase of absolute NK cell numbers >1000 cells/mcL in ≥80% of patients.

- Ch14.18/CHO concentrations [Designated as safety issue: No]
- Anti-tumour response [Designated as safety issue: No]

  Anti-tumour response in patients with measureable disease (bone marrow, skeletal lesions, soft tissue lesions, lymph nodes and/or primary tumour site) as measured by immunocytology, MIBG, CT and/or MRI.

- Confirmation cohort [Designated as safety issue: No]

  Once the dose finding stage is completed we will recruit a further 20 patients to the same dose level to confirm the primary and secondary endpoints.

Estimated Enrollment:	60
Study Start Date:	November 2010
Estimated Study Completion Date:	December 2013
Estimated Primary Completion Date:	March 2013 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: dose schedule finding ch14.18/CHO Subcutaneous aldesleukin (IL-2) will be given at a dose of 6 x 106 IU/m2/day in two 5 day blocks (days 1-5 and 8-12). A continuous infusion of ch14.18/CHO is started on day 8. The duration of the infusion is dependent on the assigned infusion schedule. The duration will range from 10 to 21 days. Three dose levels will be considered with respect to daily dose (7 mg/m2, 10 mg/m2, 15 mg/m2), which relates to total doses of 100 mg/m2,150 mg/m2 and 210 mg/m2. Patients will receive isotretinoin (13-cis-RA) 160 mg/m²/day divided into two equal doses given orally twice a day for 14 days after the completion of the ch14.18/CHO infusion. The starting day is dependent on the duration of ch14.18/CHO infusion and may be either day 19, 23, 24 or 30.	Drug: ch14.18/CHO Other Name: Chimeric 14.18 anti-GD2 monoclonal antibody produced in Chinese hamster ovary cells Drug: Aldesleukin Other Names: • Proleukin • Interleukin-2 • IL-2 Drug: Isotretinoin Other Names: • 13-cis-Retinoic acid • 13-cis-RA

Detailed Description:

Although a lot of children and young people with neuroblastoma can be cured with current standard chemotherapy, sometimes, particularly at relapse the disease no longer responds to standard drugs. Therefore, there is a need to find new drug combinations which will act against neuroblastoma which no longer responds to standard drugs.

Ch14.18/CHO has been shown to improve the outcome of patients with neuroblastoma. However, one of the side effects of receiving ch14.18/CHO is severe pain. High doses of intravenous morphine are needed to control the pain and this means that patients must stay in hospital. Results from other clinical trials have shown that giving ch14.18/CHO over a longer time reduces pain, yet the drug still works just as well to fight the neuroblastoma. The clinical trial aims to give ch14.18/CHO over a longer time so that intravenous morphine is not needed and that this treatment regimen can ultimately be given in an outpatient setting.

Ch14.18/CHO is a monoclonal antibody. Monoclonal antibodies are made in the laboratory and are designed to bind to specific cancer cells. Ch14.18/CHO was designed to bind to neuroblastoma cells and other cancer cells that express the GD-2 antigen. The GD-2 antigen is expressed by virtually all neuroblastoma cells. An antigen is a substance that stimulates an immune response in the body by producing antibodies. Thus, when ch14.18/CHO binds to the neuroblastoma cells, the body's immune system is stimulated to attack and kill the neuroblastoma cells. Ch14.18/CHO is called chimeric, because it was genetically engineered to consist of 30% mouse-protein and of 70% human protein.

Ch14.18/CHO represents a new kind of cancer therapy that, unlike chemotherapy and radiation, targets the destruction of cancer cells without destroying nearby healthy cells. There is laboratory evidence to suggest that ch14.18/CHO can activate the body's own immune cells to destroy cancer cells. These immune cells include killer cells that are activated or stimulated by aldesleukin (IL-2). Therefore this treatment is a combination of ch14.18/CHO and aldesleukin (IL-2).

Aldesleukin (IL-2) is a substance that is similar to a substance made by the body in all individuals. Under normal circumstances, the body makes small amounts of aldesleukin (IL-2) that help white blood cells fight infection. It is now possible to make aldesleukin (IL-2) in the laboratory and give humans much higher doses than their own body makes. There is evidence in the laboratory and in animals that aldesleukin (IL-2) increases the anti-cancer effect of monoclonal antibodies like ch14.18/CHO. We wish to study whether aldesleukin (IL-2) can help improve the effectiveness of ch14.18/CHO in humans.

In addition to ch14.18/CHO and aldesleukin (IL-2), isotretinoin (13-cis-RA) will also be given. Isotretinoin (13-cis-RA) is considered standard treatment for patients with neuroblastoma and works by induction of neuroblastoma cell death.

Eligibility

Ages Eligible for Study:	1 Year to 21 Years (Child, Adult)
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- At study entry patients must be > 1 year but <= 21 years of age. NOTE: Patients >21 years but <= 45 years of age, fulfilling the remaining criteria, may be enrolled in the study. These patients will be analysed separately and will not be included in the dose finding schedule algorithm. The purpose for inclusion of the older patients is to enable the collection of tolerability data.
- Patients must be diagnosed with neuroblastoma according to the INSS criteria.
- Must have received at least one previous high dose treatment followed by stem cell rescue after conventional therapy.
- Must fulfil one of the following criteria:
- Patients with stage 4 neuroblastoma on the current high-risk SIOPEN trial (HR-NBL-1/SIOPEN) either with primary refractory disease having had more than two front-line treatments or patients ineligible for the R2 randomization due to major delays after completed high-dose treatments.
- Treated and responding relapse after primary stage 4 disease, without signs of progression at study entry
- Treated and responding disseminated relapse after primary localized neuroblastoma without signs of progression at study entry.
- Patients must have a performance status greater or equal 70% (Lansky Score or Karnofsky, see Appendix 1: performance Scales , page 91)
- Patients must have an estimated life expectancy of at least 12 weeks.
- Patients must consent to the placement of a central venous line, if one has not already been placed.
- Patients must be off any standard or experimental treatments for at least two weeks prior to study entry and be fully recovered from the short term major toxic effects.
- Patients must have no immediate requirements for palliative chemotherapy, radiotherapy or surgery.
- At least 4 weeks after major surgery (e.g. laporotomy or thoracotomy) and fully recovered from any post-surgical complications.
- HIV and Hepatitis B negative.
- Females of childbearing potential must have a negative pregnancy test. Patients of childbearing potential must agree to use an effective birth control method. Female patients who are lactating must agree to stop breast-feeding.
- Patients may have had prior CNS metastasis providing the following criteria are all met:
- the patient's CNS disease has been previously treated,
- the patient's CNS disease has been clinically stable for four weeks prior to starting this study (assessment must be made clinically and by CT or MRI scan),
- the patient is off steroids for CNS disease for four weeks prior to starting on study and during the course of the study.
- Patients with seizure disorders may be enrolled if on anticonvulsants and are well controlled.
- All patients and/or their parents or legal guardians must sign a written informed consent
- All institutional and national requirements for human studies must be met.
- Laboratory Testing:
- Patients should have a shortening fraction of >= 30 % by Echocardiogram.
- Patients should have FEV1 and FVC >60% of the predicted by pulmonary function tests. Children unable to do PFTs should have no dyspnea at rest and a pulse oximetry >94% on room air.

- All patients must have adequate bone marrow function as defined by ANC >1 10^9/L, platelets >= 50 10^9/L and haemoglobin > 9.0 g/dL.
- Patients must have adequate liver function, as defined by an ALT or AST < 5 x normal and a total bilirubin < 1.0 mg/dL.
- Patients must have adequate renal function, as defined by a serum creatinine <1.5 mg/dL or a creatinine clearance or radioisotope GFR of > 60 mL/minute/1.73m2.

Exclusion Criteria:

- Patients with progressive disease
- Patients who have previously received treatment with ch14.18/SP2/0 and/or ch14.18/CHO.
- Platelet transfusion dependent.
- Patients with significant intercurrent illnesses and/or any of the following:
- Patients with symptoms of congestive heart failure or uncontrolled cardiac rhythm disturbance.
- Patients with significant psychiatric disabilities or uncontrolled seizure disorders.
- Patients with active infections.
- Patients with a clinically significant neurologic deficit or objective peripheral neuropathy (Grade >2) are ineligible.
- Patients with clinically significant, symptomatic, pleural effusions.
- Patients who require, or are likely to require, corticosteroid or other immunosuppressive drugs.
- Concurrent treatment with any non-trial anticancer therapies.

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: NCT01701479

Locations

Austria

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Investigators

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More Information

Additional Information:

Related Info EXIT

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Responsible Party:	St. Anna Kinderkrebsforschung
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Health Authority:	Austria: Agency for Health and Food Safety Germany: Paul-Ehrlich-Institut France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Israel: Ministry of Health Italy: Ethics Committee Spain: Agencia Española de Medicamentos y Productos Sanitarios United Kingdom: Medicines and Healthcare Products Regulatory Agency

Keywords provided by St. Anna Kinderkrebsforschung:
Neuroblastoma
Refractory neuroblastoma
Relapsed neuroblastoma
ch14.18/CHO
Aldesleukin (IL-2)

Additional relevant MeSH terms:

Neuroblastoma	Isotretinoin
Neuroectodermal Tumors, Primitive, Peripheral	Antineoplastic Agents
Neuroectodermal Tumors, Primitive	Analgesics, Non-Narcotic
Neoplasms, Neuroepithelial	Analgesics
Neuroectodermal Tumors	Sensory System Agents
Neoplasms, Germ Cell and Embryonal	Peripheral Nervous System Agents
Neoplasms by Histologic Type	Physiological Effects of Drugs
Neoplasms	Anti-HIV Agents
Neoplasms, Glandular and Epithelial	Anti-Retroviral Agents
Neoplasms, Nerve Tissue	Antiviral Agents
Aldesleukin	Anti-Infective Agents
Interleukin-2	Immunologic Factors
Antibodies, Monoclonal	Dermatologic Agents

ClinicalTrials.gov processed this record on November 25, 2016