LEUKEMIA & LYMPHOMA SOCIETY®

Erdheim-Chester Disease

No. 37 in a series providing the latest information for patients, caregivers and healthcare professionals

Highlights

- Erdheim-Chester disease (ECD) is a rare, slow-growing blood cancer and a type of histiocytosis. Histiocytosis is a disorder marked by the excessive production of histiocytes, a type of immune cell. The histiocytes invade tissues and organs and cause inflammation and damage.
- ECD tends to involve multiple organ systems in the body. Patients may experience a wide variety of symptoms. The most common symptom is pain in the long bones of the arms and legs.
- The identification of the *BRAF* V600E mutation and alterations in the MAPK (mitogen-activated protein kinase) signaling pathways have led to a greater understanding of Erdheim-Chester disease.
- For ECD patients with the *BRAF* V600E mutation, vermurafenib (Zelboraf®) is an FDA-approved oral treatment. Various other treatments are available for people who do not have the *BRAF* V600E mutation.

Introduction

Erdheim-Chester disease (ECD) is a rare, slow-growing blood cancer in which an excessive number of histiocytes (an immune cell and a form of white blood cell) build up in certain tissues and organs and damage them. Histiocytes are unlike typical white blood/immune cells in that they do not travel in the bloodstream throughout the body.

ECD most often affects the long bones of the arms and legs, but it can also affect the skin, lungs, heart, kidneys, brain, tissue behind the eyes, and the back wall of the abdomen (called the "retroperitoneum"). The symptoms can range from mild to severe and life-threatening.

ECD is a type of histiocytosis. Histiocytosis is the generic name for a group of syndromes distinguished by an abnormal increase in the number of immune cells called "histiocytes." As immune cells, histiocytes normally help protect the body from infection and injury. Other types of histiocytosis include Langerhans cell histiocytosis and Rosai-Dorfman disease.

The *BRAF* V600E gene mutation has been detected in the cells of approximately half of ECD cases. This mutation leads to excess production of a protein. This protein activates the MAPK (mitogen-activated protein kinase) signaling pathway, enhancing cell proliferation and survival, and leads to an abnormal number of histiocytes accumulating in the body's tissues and organs. This causes invasion of various organs by histiocytes, leading to inflammation (redness, swelling, pain and/or a feeling of heat in the body) and fibrosis (thickening and scarring of tissue).

This fact sheet can help people with ECD learn more about its diagnosis and treatment and provides helpful resources for more information. Please visit *Health Terms* on page 9 for a better understanding of certain terms used in this publication.

Signs and Symptoms

A "sign" is a change in the body that the doctor sees in an examination or a test result. A "symptom" is a change in the body that a patient can see and/or feel.

The signs and symptoms of ECD vary depending on the location of the disease and extent of involvement of the internal organs. Patients may exhibit a diverse group of manifestations. Bone pain is the most common symptom. Signs and symptoms may include:

- Bone pain in the long bones of the legs and arms
- Abdominal or lower back pain
- Reduced kidney function and painful or difficult urination
- Skin rash
- Difficulty with coordination and balance, including staggering gait, or slurred speech
- Pain or redness of the eyes, bulging eyes, yellow bumps on the eyelids
- Vision difficulties

- Behavior disorders
- Dry cough
- Excessive thirst and urination (See: diabetes insipidus in *Health Terms* on page 9)
- Shortness of breath and fatigue
- Swelling of the feet, ankles, and lower legs
- Weight loss
- Fever
- Muscle and joint aches
- Night sweats
- Frequent infections

Diagnosis

A diagnosis of ECD requires a thorough clinical evaluation, including a medical history, a variety of laboratory and imaging tests, and biopsies. A tissue biopsy is recommended to check for the *BRAF* V600E gene mutation.

Laboratory tests may include:

- **Complete blood count with differential**—a comprehensive blood test used to measure and analyze the cells in your blood (red blood cells, white blood cells and platelets) and their characteristics. A differential measures the various types of white blood cells in the sample, such as neutrophils, lymphocytes, monocytes, eosinophils, and basophils.
- **Comprehensive metabolic panel**—a blood test with 14 different measurements. It can detect a range of abnormalities in blood sugar and nutrient balance and evaluate liver and kidney health.
- **C-reactive protein**—a blood test used to measure the amount of C-reactive protein (CRP) in your blood. CRP levels can indicate the presence and severity of inflammation in the body.
- **Morning urine**—a test of your urine first thing in the morning to check its appearance, concentration, and content. Increased levels of protein in the urine can be a sign of kidney disease.
- **Serum osmolality**—a test used to measure the concentration of dissolved particles in your blood or urine that may signal fluid or electrolyte imbalance, including dehydration or diabetes insipidus. (Note: diabetes insipidus is different from diabetes mellitus which is common and requires insulin injections. See diabetes insipidus in *Health Terms* on page 9.)
- **Morning serum cortisol with ACTH (adrenocorticotropic hormone)**—a test taken first thing in the morning and used to determine if the adrenal glands are producing an appropriate amount of the hormone called "cortisol" in the blood, urine, or saliva. Cortisol testing can help diagnose or rule out certain conditions.
- **FSH (follicle-stimulating hormone) and LH (luteinizing hormone) with testosterone (males) and estradiol (females)**—blood tests used to evaluate functioning of the pituitary gland, as well as the health of reproductive organs
- **TSH (thyroid-stimulating hormone) and free T4 (thyroxine)**—blood tests used to see if the thyroid gland is functioning properly
- **Prolactin**—a blood test used to measure the amount of prolactin, a hormone produced by the pituitary gland
- **IGF-1 (insulin-like growth factor-1)**—a test used to measure the amount of IGF-1 in the blood and to evaluate pituitary function. Along with growth hormone, IGF-1 helps promote normal bone and tissue growth and development.
- ***BRAF* V600E genotyping**—the process of testing a sample of tissue to determine differences in genetic makeup. For example, genotyping can check for the *BRAF* V600E mutation and alterations in the MAPK pathway.
- **Next generation sequencing**—a technology used for determining the sequence of DNA (deoxyribonucleic acid) or RNA (ribonucleic acid) to study genetic variations associated with disease. A tissue sample can be used to check for mutations.
- **Fusion assay**—a test to detect gene fusions (the joining of two genes) in cell lines and tissue samples

Imaging tests (which provide "pictures" of the inside of the body), and other measurement tests used to diagnose ECD, based on symptoms or organ involvement, may include:

- **CT (computed tomography) scan of the chest, abdomen, and pelvis**—an imaging test that uses x-rays to make detailed images of the inside of the body
- **PET/CT (positron emission tomography/computed tomography) scan**—an imaging test that uses a radioactive substance called a "tracer" to look for cancer cells in the body

- **MRI (magnetic resonance imaging) of the brain and heart**—an imaging test using radio waves and powerful magnets to create detailed images of the inside of the body
- **Echocardiogram (echo)**—a procedure used to check how well your heart is working. It uses high-frequency sound waves to display pictures of the heart.
- **Electrocardiogram (EKG or ECG)**—a procedure used to show the electrical activity of the heart using sensors
- **Ultrasound**—an imaging test using high-frequency sound waves to create images of the inside of the body
- **Pulmonary function tests**—a group of tests that measure how well the lungs are working
- **Bone scan**—a procedure used to check for abnormal areas or damage in the bones. A very small amount of radioactive material is injected into a vein and travels through the blood. This radioactive material collects in the bones and then is detected by a scanner.
- **X-ray imaging**—a procedure that uses high-energy radiation to take pictures of areas inside the body.

An additional test that may be used is a **biopsy**. Biopsy of the skin, bone, or soft tissue is the removal of cells or tissues for examination by a pathologist (a doctor who specializes in the microscopic study of cells and tissues). Multiple samples may be needed if there is bone decalcification (softening of the bone due to loss of calcium) in the sample.

In addition to their hematologist-oncologist (a doctor who specializes in treating cancers of the blood), patients may visit with one or more other specialist doctors including: a dermatologist (for diseases of the skin), an endocrinologist (for conditions related to glands and hormones), a nephrologist (for diseases of the kidneys), a neurologist (for disorders of the nerves and nervous system), an ophthalmologist (for diseases of the eye), or a urologist (for disorders of the reproductive and urinary systems). Consultations with providers in other areas, such as pain management, palliative (supportive) care and mental health care, may also be useful.

Visit www.LLS.org/booklets to view *Understanding Lab and Imaging Tests* and *Understanding Genetics* for more information.

To help you visualize and better understand certain tests and processes, visit www.LLS.org/3D to view the interactive 3D model library.

Treatment

Not all ECD patients require treatment at the time of diagnosis. For patients who don't have symptoms, a period of observation is suggested. For patients with symptoms, such as bone pain, central nervous system (CNS) involvement or organ dysfunction, treatment is necessary. Treatment is individualized based on a patient's clinical characteristics, disease mutational status, fitness level, and several other factors.

The US Food and Drug Administration (FDA) approves drugs for certain health conditions. Some drugs that are not FDA-approved to treat ECD can be used as an "off-label" treatment. "Off-label" prescribing is when a doctor gives a drug that is FDA-approved to treat one condition for another condition, if the doctor feels it will benefit the patient. This is a common practice.

Your healthcare provider will discuss your treatment options, including possible participation in a clinical trial. It is important to see a hematologist-oncologist who has experience in treating ECD. Another option is going to a hematologist-oncologist who consults with an ECD expert at a major cancer center.

Below are various treatment options available to ECD patients.

Kinase inhibitors

These drugs block the action of enzymes called "kinases." Kinases are involved in cell signaling, cell growth, and cell division.

- **Vemurafenib (Zelboraf®)**—FDA-approved for the treatment of Erdheim-Chester disease with the *BRAF* V600 mutation; taken by mouth
- **Dabrafenib (Tafinlar®)**—for patients with unresectable or metastatic melanoma with the *BRAF* V600E or *BRAF* V600K mutation as detected by an FDA-approved test; taken by mouth

Immunotherapy

These drugs encourage the immune system to work more effectively.

- **Interferon alfa (Intron A®)**—interferes with the ability of cancer cells to divide. It may be administered with oral prednisone. Pegylated interferon has a substance attached to it to help it stay in the body longer. It is given by injection.

MEK inhibitors

These drugs block proteins called "MEK1 and MEK2," which help control cell growth and survival.

- **Cobimetinib (Cotellic®)**—FDA-approved for the treatment of patients with unresectable or metastatic melanoma with a *BRAF* V600E or V600K mutation, in combination with vemurafenib; taken by mouth
- **Trametinib (Mekinist®)**—FDA-approved as a single agent for the treatment of BRAF-inhibitor treatment-naïve patients with unresectable or metastatic melanoma with a *BRAF* V600E or V600K mutation as detected by an FDA-approved test; taken by mouth

Interleukin-1 receptor antagonists

These drugs are composed of related proteins made by leukocytes (white blood cells) and other cells in the body. Interleukins made in the laboratory are used as biological response modifiers to boost the immune system in cancer therapy. Interleukin antagonists work to reduce swelling and to suppress the immune system.

- **Anakinra (Kineret®)**—FDA-approved to treat rheumatoid arthritis as well as deficiency of an interleukin-1 receptor antagonist (DIRA), a rare autoinflammatory disease; given by injection
- **Tocilizumab (Actemra®)**—FDA-approved for rheumatoid arthritis and certain other conditions; administered by intravenous (IV) infusion or by injection under the skin

mTOR inhibitors

These drugs block the activity of the mammalian target of a protein kinase called "rapamycin," which regulates growth factors that stimulate both cell growth and growth of new blood vessels (called "angiogenesis").

- **Sirolimus (Rapamune®)**—FDA-approved for the prophylaxis (prevention) of organ rejection in patients with renal transplants or for the treatment of patients with a condition affecting the lungs, kidneys, and lymphatic system (called "lymphangioleiomyomatosis"); taken by mouth
- **Everolimus (Afinitor®)**—FDA-approved for breast cancer, pancreatic cancer, renal cell carcinoma, and certain other indications; taken by mouth

Tyrosine kinase inhibitors

These drugs block the action of enzymes called "tyrosine kinases," preventing cancer cells from growth and division.

- **Imatinib mesylate (Gleevec®)**—FDA-approved for patients with chronic myeloid leukemia (CML), Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL), and other conditions; taken by mouth

Chemotherapy

These drugs damage the DNA (deoxyribonucleic acid) or RNA (ribonucleic acid) in cancer cells and interfere with their ability to grow or multiply.

- **Methotrexate (various brands)**—used to treat certain cancers, rheumatoid arthritis, and severe psoriasis; taken by mouth
- **Cladribine (Leustatin®)**—used to treat certain leukemias, lymphomas, and a type of histiocytosis called "Langerhans cell histiocytosis"; administered by intravenous (IV) infusion

Tumor necrosis factor-alpha inhibitors

These drugs work by blocking the action of TNF-alpha, a substance in the body that causes inflammation.

- **Infliximab (Remicade®)**—used to relieve the symptoms of certain autoimmune disorders, such as rheumatoid arthritis and Crohn's disease; administered by intravenous (IV) infusion

Corticosteroids

These drugs are hormones made in the adrenal cortex (part of the adrenal gland in the body) or manufactured in a laboratory. They are used for numerous purposes in the treatment of cancer. For example, corticosteroids can decrease inflammation, alter the body's normal immune system responses, cause programmed cell death, and stimulate appetite.

- **Prednisone** (various brands)—can be used alone or in combination with other drugs; taken by mouth in pill or liquid form

Surgery and radiation therapy

These treatments have limited roles in the management of ECD. If a mass develops as a result of ECD, surgical removal may be recommended. Radiation may be used to help with bone pain associated with ECD lesions (abnormal tissues).

Participation in a clinical trial

Taking part in a research study called a "clinical trial" is an appropriate treatment choice for many patients. The treatments listed above may be used in current clinical trials. Discuss this option with your healthcare provider or contact an LLS Information Specialist for more information. See also *Clinical Trials for Blood Cancers* on page 5 for details.

Treatment Side Effects

Side effects depend on many factors, including the type of treatment and dosage, and the patient's age and coexisting medical conditions. Treatment may cause fever or chills, fatigue, nausea, loss of appetite, mouth sores, peripheral neuropathy (tingling, burning, numbness or pain in the hands and/or feet), changes in blood cell counts, infection, rash, vomiting, diarrhea, shortness of breath, swelling, temporary loss of hair, and other side effects.

Side-effect management is important. If you have any concerns about potential side effects, talk to the members of your healthcare team to get help. Most side effects can be managed without compromising the effectiveness of your treatment. In fact, talking to your healthcare team about your side effects often leads to better treatment outcomes. Most side effects are temporary and resolve when treatment is completed. However, long-term side effects or "late effects" may appear years after the treatment has been completed. Late side effects may include development of another type of cancer, heart disease, hypothyroidism (low levels of thyroid hormones), and loss of fertility.

Visit www.LLS.org/booklets and Filter by Topic (Side Effect Management) for more information.

Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called "clinical trials" and they are used to find better ways to care for and treat people who have cancer.

In the United States, the FDA requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer. Researchers use cancer clinical trials to study new ways to:

- Treat cancer using:
  - A new drug
  - A drug that has been approved, but to treat a different kind of cancer ("off-label" use)
  - A new combination of drugs
  - A new way of giving a drug—by mouth, intravenously (IV), etc.
- Manage cancer signs and/or symptoms and ease treatment side effects
- Find and diagnose cancer
- Keep cancer from coming back (recurring) after treatment
- Manage long-term side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, innovative therapies, and provide helpful information for future patients. The treatments and information we have today are due in large part to patients being willing to join clinical trials. Anyone interested in being part of a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit www.LLS.org/WhatToAsk for lists of suggested questions).
- Ask a family member or friend to go with you when you see your doctor—both for support and to take notes.

Clinical trials can be difficult to understand and to navigate, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome the barriers to enrollment and provide support throughout the entire clinical-trial process. Our Clinical Trial Nurse Navigators are registered nurses who are experts in blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals.
- Help you understand the clinical-trial process, including your rights as a patient.
- Ask you for details about your diagnosis (such as past treatments, treatment responses, and your cancer genetic profile), your current health, and your medical history, because these might impact whether you can take part in certain clinical trials.
- Help you understand how your finances, insurance coverage, support network, and ability and willingness to travel might impact your choice of clinical trials.
- Guide and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites.
- Help deal with any problems you might have as you enroll in a trial.
- Support you throughout the clinical-trial process.

Please call an LLS Information Specialist at (800) 955-4572 or visit www.LLS.org/CTSC for more information about clinical trials and the Clinical Trial Support Center at LLS.

Also, visit www.LLS.org/booklets to view *Understanding Clinical Trials for Blood Cancers.*

Participation in a Disease Registry

Patients can help researchers gain a better understanding of ECD and help in the development of new therapies by participating in a disease registry. A disease registry collects, manages, and analyzes information on a particular diagnosis over time. This may include collecting information about blood and tissue samples, blood counts, symptoms, treatments, medical history, and family medical history. For more information, please refer to the ECD Global Alliance listing in the *Resources* section on page 8.

Incidence, Causes and Risk Factors

ECD was first described by the scientists Erdheim and Chester in 1930. More than 1,500 cases have been reported worldwide. (see Harouche J, et al. in *References*) Because ECD is so rare and difficult to diagnose, it may be under-diagnosed or misdiagnosed. It is most often diagnosed in adults during middle age; it is very rare in children. There are slightly more males than females diagnosed with ECD.

In 2016, the World Health Organization (WHO) recognized ECD as histiocytic neoplasm (cancer).

Increasing awareness and improvements in diagnostic precision will provide more accurate data in the future on the incidence (the number of people in a population who develop the disease over a specific period of time, in other words, "new cases") and prevalence (the number of people in a population who have the disease at a specific time, in other words, "all cases") of ECD. As clinicians and researchers continue to learn about this complex disease, updated guidelines have become necessary.

The National Comprehensive Cancer Network (NCCN), an alliance of leading cancer centers, recently published clinical practice guidelines for the three most common forms of histiocytosis in adults: Erdheim-Chester disease, Langerhans cell histiocytosis, and Rosai-Dorfman disease.

Among patients with ECD, there is an increased incidence of myeloid neoplasms, which include myeloproliferative neoplasms (MPNs), myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML), or MDS/MPN overlap syndrome. Erdheim-Chester disease can also occur along with other histiocytic neoplasms.

While the exact cause of ECD is unknown, more than half of people with ECD have a specific mutation in the *BRAF* V600E gene on the histiocytic cells (or their precursor cells). This mutation leads to the production of proteins with genetic alterations in the MAPK (mitogen-activated protein kinase) signaling pathway, which controls many cell functions. These abnormal proteins lead to unregulated cell growth and division, causing an excessive number of histiocytes to accumulate in the body's tissues and organs. *BRAF* V600E is a somatic mutation, meaning the change in the DNA of the cells occurred during a person's lifetime, and cannot be passed on to children.

Follow-Up

A clinical evaluation is recommended every three to six months, or more frequently as symptoms or organ dysfunction require. Patients should be checked for central nervous system and organ involvement. Tests may include laboratory studies, imaging, electrocardiogram (looks for abnormalities in the heart's electrical impulses using electrodes), echocardiogram (checks for irregularities in the heart's structure using ultrasound), and bone marrow examination.

The NCCN Clinical Practice Guidelines for healthcare providers suggest:

- PET/CT scans to monitor disease response once treatment is started
- Organ-specific imaging (eg, CT or MRI), as needed
- Regular skin examination
- Electrocardiogram (ECG)
- Evaluation for pituitary hormone abnormalities

Outcomes

The course of ECD varies based on the site of disease and treatment response. Some patients live with a good quality of life. Others may experience serious complications such as pulmonary fibrosis (scarring of lung tissue), heart failure or kidney impairment. While treatment may control symptoms and growth of the disease, there is no known cure. Research is ongoing to better understand the biology and treatment of ECD.

Acknowledgement

The Leukemia & Lymphoma Society appreciates the review of this material by

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We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the United States and in Canada. To find the chapter nearest to you, visit our website at www.LLS.org/ChapterFind or contact an Information Specialist at (800) 955-4572.

LLS offers free information and services for patients and families touched by blood cancers. This section lists various resources available to you. Use this information to learn more, to ask questions, and to make the most of your healthcare team.

For Help and Information

Consult with an Information Specialist. Information Specialists are highly trained oncology social workers, nurses and health educators. They offer up-to-date information about disease, treatment and support. Language services are available. For more information, please:

- Call: (800) 955-4572 (Monday through Friday, 9 am to 9 pm ET)
- Email and Live chat: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical-trial process. Please visit www.LLS.org/CTSC for more information.

One-on-One Nutrition Consultations. Access free one-on-one nutrition consultations provided by a registered dietitian with experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management, and survivorship nutrition. They also provide additional nutrition resources. Please visit www.LLS.org/nutrition for more information.

Free Information Booklets. LLS offers free education and support booklets that can either be read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial support, including insurance premium and medication co-pay assistance, to eligible individuals with blood cancer. For more information, please:

- Call: (877) 557-2672
- Visit: www.LLS.org/finances

LLS Health Manager™ App. This free mobile app helps you manage your health by tracking side effects, medication, food and hydration, questions for your doctor, and more. Export the information you've tracked in a calendar format and share it with your doctor. You can also set up reminders to take medications, hydrate, and eat. Please visit www.LLS.org/HealthManager to download for free.

LLS Coloring for Kids™. This free coloring app allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. The app includes blank canvases, general coloring pages and pages from LLS coloring books. This app can be used anywhere and may help pass the time in waiting rooms or during treatment. Please visit www.LLS.org/ColoringApp to learn more and download.

Podcast. *The Bloodline* with LLS is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Please visit www.LLS.org/TheBloodline for more information and to subscribe.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Please visit www.LLS.org/SuggestedReading to find out more.

Community Resources and Networking

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Please visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients reach out and share information. Please visit www.LLS.org/chat for more information.

LLS Chapters. LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection® Program* (a peer-to-peer support program), local support groups and other great resources. For more information about these programs or to contact your chapter, please:

- Call: (800) 955-4572
- Visit: www.LLS.org/ChapterFind

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to view the directory.

Advocacy. The LLS Office of Public Policy (OPP) enlists volunteers to advocate for policies and laws to speed new treatments and improve access to quality medical care. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy

Additional Help for Specific Populations

Información en Español (LLS information in Spanish). Please visit www.LLS.org/espanol for more information.

Language Services. Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs. For more information, please

- Call: the VA (800) 749-8387
- Visit: www.publichealth.va.gov/exposures/AgentOrange

World Trade Center Survivors. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA, crashes

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

People Suffering from Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a 2-week period. For more information, please:

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov and enter “depression” in the search box

Resources

ECD Global Alliance

https://erdheim-chester.org/

The ECD Global Alliance is dedicated to awareness, support, education, and research related to Erdheim-Chester disease. Includes information about clinical trials, physician and care center referrals, and a patient registry.

Histiocytosis Association

https://histio.org/

856-589-6606

The Histiocytosis Association is dedicated to raising awareness about histiocytic disorders, providing educational and emotional support, and funding research leading to better treatments and a cure. The Association offers information about clinical trials, a physician directory, and a search tool for resources.

National Comprehensive Cancer Network (NCCN)

https://www.nccn.org/

215-690-0300

NCCN is a non-for-profit alliance of 32 leading cancer centers devoted to patient care, research, and education. Visit the website to reach the healthcare professional guidelines. (The patient version of NCCN Clinical Practice Guidelines for Histiocytic Neoplasms is not yet available.)

National Organization for Rare Disorders (NORD)

www.rarediseases.org

(800) 999-6673 / (203) 744-0100

The National Organization for Rare Disorders is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. It is committed to the identification, treatment and cure of rare disorders through programs of education, advocacy, research and service.

Health Terms

Diabetes Insipidus. An uncommon disorder that causes an imbalance of fluids in the body. This imbalance leads to the production of large amounts of urine as well as extreme thirst. While the terms "diabetes insipidus" and "diabetes mellitus" sound similar, they are not related. Diabetes mellitus is common and often referred to simply as "diabetes," for which patients take insulin. Diabetes mellitus involves high blood sugar levels and can occur as type 1 or type 2.

Disease Registry. A disease registry collects information on patients with a particular diagnosis to help researchers better understand the disease and develop new therapies.

Fibrosis. Fibrosis means the scarring and thickening of any tissue or organ.

Histiocyte. This is a type of immune cell found in many organs and tissues. Histocytes help the immune system destroy foreign substances to protect the body from infection.

Histiocytosis. The term for a group of rare disorders in which too many histiocytes (immune cells) build up in certain tissues and organs, including the skin, bones, spleen, liver, lungs, and lymph nodes. This can cause damage to tissue, and/or cause tumors to form in one or more parts of the body. The tumor may be benign (not cancerous) or malignant (cancerous).

Immunotherapy. A type of therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases.

Langerhans Cell Histiocytosis (LCH). A rare blood cancer that forms when a type of white blood cell called a "Langerhans cell" becomes abnormal and grows in different parts of the body. LCH is most common in young children but can occur at any age.

Neoplasm. An abnormal mass of tissue that forms when cells grow and divide more than they should, or do not die when they should. Neoplasms may be benign (not cancer) or malignant (cancer). Benign neoplasms may grow large but do not spread into, or invade, nearby tissues or other parts of the body. Malignant neoplasms can spread into, or invade, nearby tissues. They can also spread to other parts of the body through the blood and lymph systems. Neoplasm is another word for "tumor."

Rosai-Dorfman Disease (RDD). A rare disease in which the body produces too many histiocytes in the lymph nodes. The histiocytes most commonly accumulate in the neck, though other lymph nodes and parts of the body may also be affected.

Targeted Therapy. The use of drugs or substances that block the growth and spread of cancer by interfering with specific molecules. A goal of targeted therapy is to leave normal, healthy cells mostly intact. Therapies may be combined.

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FS37 6/22