KANUMA® (SEBELIPASE ALFA)

KANUMA® (SEBELIPASE ALFA) OVERVIEW

Kanuma is an innovative enzyme therapy approved for the treatment of patients with a diagnosis of lysosomal acid lipase deficiency (LAL-D).[1] LAL-D is a genetic, chronic and progressive ultra-rare metabolic disease associated with multi-organ damage in infant, pediatric, and adult patients, and premature death in infants.[2]

Kanuma is the first therapy to address the underlying cause of LAL-D. By replacing deficient LAL, treatment with Kanuma reduces the accumulation of fatty materials (cholesteryl esters and triglycerides) in the lysosomes of cells throughout the body. Kanuma is administered via intravenous infusion.[1]

Prior to Kanuma, historical approaches to the management of LAL-D did not address the underlying enzyme deficiency responsible for the devastating outcomes of the disease.[2,3] No controlled clinical trials have proven these approaches, including lipid-lowering medications, liver transplant, and hematopoietic stem cell transplantation, to be safe or effective in treating patients with LAL-D.[2-4,7,8]

* Based on modeling, using a subset of 31 patients (≥5 years of age) in an observational study who received a liver biopsy, and 1 additional patient with no biopsy who received a liver transplant. Patients selected by their clinician for liver biopsy are expected to have more evidence of disease progression than patients with LAL-D overall..

ABOUT LAL-D

In patients with LAL-D, deficient LAL enzyme activity results in continuous accumulation of cholesteryl esters and triglycerides in multiple organs, including the liver, spleen, gastrointestinal tract, and the walls of blood vessels. This can result in progressive, multi-organ damage, including fibrosis, cirrhosis, liver failure, and other devastating consequences.[2,3]

- In infants, LAL-D is a rapidly progressive and imminently fatal disease characterized by profound malabsorption, growth failure, liver fibrosis, cirrhosis, and liver failure. The median age of death in infants with LAL-D is 3.7 months.[4]
- In an observational study, approximately 50% of pediatric and adult patients with LAL-D progressed to fibrosis, cirrhosis, or liver transplant within 3 years of clinical manifestation onset.*[5]
- Published literature on 135 LAL-D cases showed that 51% progressed to fibrosis, cirrhosis, or death.[2]

CLINICAL TRIAL DATA

The efficacy of Kanuma is based on data from 75 patients (including infant, pediatric, and adult patients) with LAL-D who were treated with Kanuma in two clinical studies and one supporting open-label extension study.[1]

Kanuma in Infants with Rapidly Progressive LAL-D

In a multicenter, open-label study in 9 infant patients with LAL-D (who presented with growth failure or other evidence of rapidly progressive disease within the first 6 months of life), patients treated with Kanuma had significantly improved survival compared with a historical cohort of untreated infants with LAL-D.

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ALEXION®

- Of the 9 infants treated with Kanuma, 6 survived beyond 12 months of age (67%) compared to 0 of 21 (0%) in the historical cohort, all of whom died by 8 months of age. The median age of the 6 surviving Kanuma-treated patients was 18.1 months (12 to 42.2 months).[1]
- Weight z-scores improved in all patients after initiation of Kanuma treatment, with further improvements demonstrated following dose escalation.[1]

Kanuma in Pediatric and Adult Patients with LAL-D

In a multicenter, double-blind, placebo-controlled study in 66 pediatric and adult patients (ages 4 to 58 years) with LAL-D, known as the ARISE study, over a 20-week period:[1,6]

- Patients treated with Kanuma had larger reductions from baseline in ALT values and liver fat content, as measured by MRI, compared to patients treated with placebo. In addition, patients treated with Kanuma had a 32% reduction in mean liver fat content compared with a 4% reduction in placebo patients ($p<0.0001$).[1,6]
- 31% of patients treated with Kanuma achieved ALT values <ULN[†] compared with 7% of placebo patients ($p=0.0271$).[1,6] In all patients with elevated ALT values at baseline (82 of 84 patients in clinical trials), reductions in ALT values were observed, generally within 2 weeks after initiation of treatment with KANUMA.[1]
- The significance of these findings as they relate to progression of liver disease in LAL deficiency has not been established.[1]

Improvements in dyslipidemia were also observed over a 20-week period:[1,6]

- Patients treated with Kanuma had a 28% reduction in mean LDL-c from baseline compared with a 6% reduction in placebo patients ($p<0.0001$).[1,6]
- Patients treated with Kanuma had a 25% reduction in mean triglycerides from baseline compared with an 11% reduction in placebo patients ($p=0.0357$).[1,6]
- Patients treated with Kanuma had a 19% increase in mean HDL-c from baseline compared with a 1% decrease in placebo patients ($p<0.0001$).[1,6]
- The effect of Kanuma on cardiovascular morbidity and mortality has not been established.[1]

In a subsequent open-label extension study including all but one original study participant (65/66), patients who were treated with Kanuma for up to 36 weeks demonstrated improvements in lipid parameters, including LDL-c and HDL-c, as well as ALT.

[†] The upper limit of the normal range (ULN) was defined as 34 U/L for female patients 4 to 69 years of age and male patients 4 to 10 years of age and as 43 U/L for male patients 10 to 69 years of age.

KANUMA ACCESS & SUPPORT

Alexion's objective is that every patient with LAL-D who can benefit from Kanuma will have access to it. As part of this commitment, Alexion offers personalized support to LAL-D patients though its OneSource™ program. Each LAL-D patient has a dedicated OneSource nurse case manager who can help patients and their families understand their insurance benefits and provide information about reimbursement assistance. Alexion also offers a co-pay assistance program for eligible patients with commercial insurance. Our Alexion nurse case managers can also share information on nonprofit independent foundations that provide both financial and treatment-related support for all patients, regardless of their type of insurance. For patients who cannot obtain access to Kanuma, the Alexion Access Foundation, a charitable foundation, provides Kanuma free of charge to qualifying patients in need.

Patients, caregivers, and healthcare providers in the United States can call 1.888.765.4747 to speak with a OneSource case manager.

For more information about Kanuma, visit Kanuma.com.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions Including Anaphylaxis

Hypersensitivity reactions, including anaphylaxis, have been reported in KANUMA-treated patients. In clinical trials, 3 of 106 (3%) patients treated with KANUMA experienced signs and symptoms consistent with anaphylaxis. These patients experienced reactions during infusion with signs and symptoms including chest discomfort, conjunctival injection, dyspnea, generalized and itchy rash, hyperemia, swelling of eyelids, rhinorrhea, severe respiratory distress, tachycardia, tachypnea, and urticaria. Anaphylaxis has occurred as early as the sixth infusion and as late as 1 year after treatment initiation.

In clinical trials, 21 of 106 (20%) KANUMA-treated patients, including 9 of 14 (64%) infants and 12 of 92 (13%) pediatric patients, 4 years and older, and adults experienced signs and symptoms either consistent with or that may be related to a hypersensitivity reaction. Signs and symptoms of hypersensitivity reactions, occurring in two or more patients, included abdominal pain, agitation, fever, chills, diarrhea, eczema, edema, hypertension, irritability, laryngeal edema, nausea, pallor, pruritus, rash, and vomiting. The majority of reactions occurred during or within 4 hours of the completion of the infusion. Patients were not routinely pre-medicated prior to infusion of KANUMA in these clinical trials.

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Due to the potential for anaphylaxis, appropriate medical support should be readily available when KANUMA is administered.

Hypersensitivity to Eggs or Egg Products
Consider the risks and benefits of treatment in patients with known systemic hypersensitivity reactions to eggs or egg products.

Adverse Reactions
The most common adverse reactions are: In Patients with Rapidly Progressive Disease Presenting within the First 6 Months of Life (≥30%): diarrhea, vomiting, fever, rhinitis, anemia, cough, nasopharyngitis, and urticaria. In Pediatric and Adult Patients (≥8%): headache, fever, oropharyngeal pain, nasopharyngitis, asthenia, constipation, and nausea.

Please see full prescribing information for Kanuma.

References

1. Kanuma (sebelipase alfa) injection. Prescribing Information. Alexion Pharmaceuticals, Inc. Initial U.S. Approval: 2015.
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4. Jones SA et al. Rapid progression and mortality of lysosomal acid lipase deficiency presenting in infants. Genetics in Medicine. 27 August 2015. doi:10.1038/gim.2015.108
5. Data on file. Study LAL-2-NH01
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8. Tolar J, Petryk A, Khan K, et al. Long-term metabolic, endocrine, and neuropsychological outcome of hematopoietic cell transplantation for Wolman disease. Bone Marrow Transplant. 2009;43:21–7. doi: 10.1038/bmt.2008.273.