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**BARE YOUR RARE**
bareyourrare.org

PATIENT & CAREGIVER GUIDE

# Erdheim-Chester Disease (ECD)

***A histiocytic neoplasm with a targetable driver — and a generous community of patient-experts.***

Built from the 2016 WHO classification, the VE-BASKET trial, MSKCC and Mayo consensus guidelines, and the lived experience of the ECD patient community. Designed to be printed, marked up, and brought to every visit.

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**1,500–2,000**
documented cases worldwide

**BRAF V600E**
found in ~50–62% of patients

**>80–95%**
carry targetable MAPK/ERK mutations
— treatment is targeted, not generic


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A NOTE FROM THE FOUNDER

# For the ones who became their own experts.

There's a particular kind of patient that Erdheim-Chester Disease tends to create. Because ECD is so rare, most people who receive this diagnosis quickly realize they are going to have to become deeply, almost professionally, informed about their own condition.

Your GP likely hasn't seen it. Your local oncologist may be consulting literature they've never had reason to read before. The path to diagnosis was probably long, strange, and full of wrong answers. And somewhere along that path, you became an expert — not because you wanted to, but because you had no choice.

That expertise deserves a home. A place where what you've learned through years of navigating this condition can help someone who was just diagnosed last week.

ECD sits at a strange intersection — classified as a histiocytic neoplasm (a slow-growing blood cancer), capable of affecting almost any organ system, with treatment protocols still being shaped in real time by the patients and researchers living and working with it. The community that exists around ECD is small but remarkably informed, and remarkably generous with that information.

I want this to be a space that reflects that generosity. My condition is Hajdu-Cheney Syndrome — another condition so rare that most doctors encounter it only in textbooks. You deserve a space that's yours, not scattered across corners of the internet.

**— Thomas Cheesman**, Founder, Bare Your Rare

SECTION 01

# Key Facts About ECD

Three facts reshape how ECD is understood today. A decade ago, most of this was unknown. Today, they change everything about how the disease is diagnosed and treated.

### C A Clonal Neoplasm

Classified by the WHO in 2016 as a histiocytic neoplasm — a slow-growing blood cancer driven by somatic mutations in immune cells. Not inherited. Not contagious. Not passed to children. The 2016 reclassification was a turning point because it legitimized research funding and insurance coverage.

### M Multi-System Disease

ECD can infiltrate bones, heart, blood vessels, kidneys, lungs, brain, eyes, and skin. The "hairy kidney" (perinephric fat infiltration) and "coated aorta" (periaortic soft tissue) on imaging scans are hallmark signatures your radiologist may recognize. Bilateral femoral cortical sclerosis is another classic radiographic finding.

### T A Targetable Driver

Over 80–95% of ECD patients carry mutations in the MAPK/ERK signaling pathway. Once you know your mutation status, treatment becomes targeted and dramatically more effective. This is the single most important fact in modern ECD care.

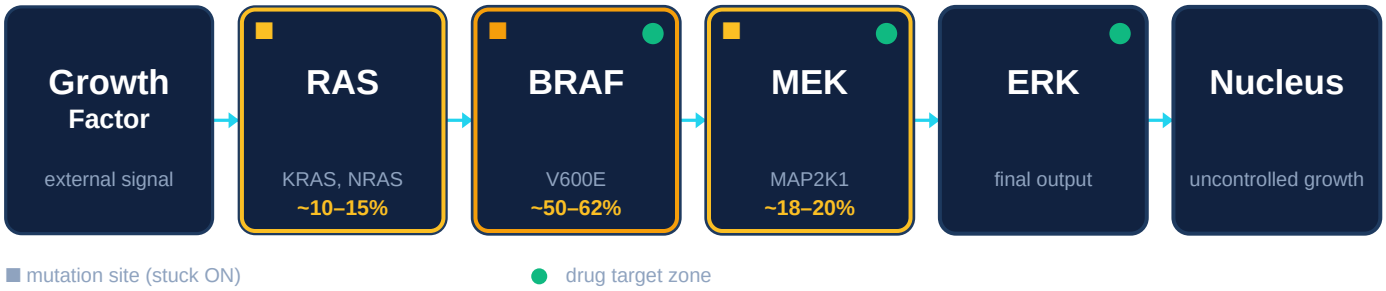
| ~1,500–2,000 | >80–95% | 2017 |
|---|---|---|
| documented cases worldwide | carry targetable MAPK/ERK mutations | first targeted therapy approved (vemurafenib) |

SECTION 02

# The Science — The MAPK/ERK Pathway

Think of the MAPK/ERK pathway (also called the RAS-RAF-MEK-ERK pathway) as your cells' internal growth-control switchboard. It is a precise chain of proteins that carries signals from receptors on the cell surface all the way to the cell's nucleus — telling cells when to grow, when to divide, and when to hold still.

***The MAPK/ERK Pathway in ECD — where mutations jam the switch ON and where drugs break the cascade.***




In ECD, somatic mutations (acquired during life, **not** inherited) create a "stuck-ON" switch. The pathway fires constantly, even without any external signal. This drives your myeloid-derived histiocytes — normal immune cells — to proliferate uncontrollably, become lipid-laden "foamy" cells, and invade tissues, causing the hallmark sclerosis, fibrosis, and organ damage you already know too well.

**The 2012 BRAF V600E discovery was the turning point.**

Before 2012, ECD was considered "inflammatory" and treated with interferon and broad immunosuppression — often with limited success. The discovery of recurrent BRAF V600E mutations proved ECD is neoplastic, not merely inflammatory. That single finding unlocked targeted therapy and fundamentally changed prognosis for most patients.

SECTION 03

# The Mutation Landscape

Knowing your specific mutation changes your treatment plan. Molecular testing (done on tissue biopsy or, increasingly, on liquid biopsy) should be part of every ECD diagnostic workup. Here is what the landscape looks like across the documented cases:

| Mutation | Frequency | Significance |
|---|---|---|
| **BRAF V600E** | **~50–62%** | Most common. Often linked to more aggressive CNS, cardiac, or orbital disease. Directly targeted by BRAF inhibitors. |
| **MAP2K1 (MEK1)** | **~18–20%** | Up to 50% of BRAF-negative cases. Sensitive to MEK inhibitors. |
| **Other MAPK genes** | **~10–15%** | KRAS, NRAS, ARAF, RAF1, and rare fusions (ALK, NTRK, CSF1R, RET). Often MEK-inhibitor responsive. |
| **Total MAPK/ERK altered** | **>80–95%** | Overall proportion of patients with a targetable driver mutation in the pathway. |
| **No detectable mutation** | **~5–10%** | Standard testing negative. Many still respond to MEK inhibitors — absence of mutation on testing is not always absence of disease biology. |

**Ask about molecular testing at diagnosis.**

If your pathology report does not include molecular testing for BRAF and the broader MAPK panel, request it. This single question redirects the entire treatment plan and can add years of effective therapy.

SECTION 04

# Targeted Therapies — How We Treat the Driver

Each drug class blocks the MAPK/ERK cascade at a different point. Which class you receive depends on your mutation — and sometimes on how your disease responds over time.

### B BRAF Inhibitors — for BRAF V600E-positive patients

Directly block the mutant BRAF protein. **Vemurafenib** was FDA-approved for ECD in 2017 — the first targeted therapy for this disease. The VE-BASKET trial provided the approval data. Related drugs: **dabrafenib**, **encorafenib**. Many patients see PET-avid lesions shrink within weeks to months.

### M MEK Inhibitors — for BRAF wild-type and other MAPK mutations

Work downstream across almost the entire pathway. Effective for patients without BRAF V600E who carry MAP2K1 or other MAPK alterations. Drugs in this class: **cobimetinib**, **trametinib**, **mirdametinib**, **binimetinib**. Cobimetinib received FDA approval specifically for ECD in 2022.

### C Combination Therapy — BRAF + MEK dual blockade

A BRAF inhibitor paired with a MEK inhibitor for deeper pathway suppression. Especially considered for aggressive or treatment-resistant disease. Common pairings: **dabrafenib + trametinib**, **vemurafenib + cobimetinib**. Dual blockade can overcome some resistance mechanisms that single-agent therapy cannot.

### E ERK Inhibitors — the emerging frontier

Block ERK directly — the very last step in the cascade before the signal reaches the nucleus. Currently in clinical trials for patients who develop resistance to upstream inhibitors. **Ulixertinib** is the most advanced candidate and is actively in Phase II trials at MSKCC and partner sites.

SECTION 05

# What Patients Report

Clinical trial data tells you what happens on average. Patient reports tell you what to expect — and what to watch for — as an individual going through targeted therapy. The consistent observations across the ECD community:

### R Rapid response is common

Many patients see PET-avid lesions shrink within weeks to months. Bone pain eases. Exophthalmos (eye protrusion) improves. "Coated aorta" and "hairy kidney" findings stabilize or regress on follow-up imaging.

### L Therapy is usually lifelong

But often at much lower doses than those used in melanoma (where these same drugs were first developed). ECD tends to respond at modest doses, and stopping therapy frequently leads to recurrence.

### D Dose reduction does not mean failure

ECD patients may be particularly sensitive to standard dosing. Dose reductions are common and do not diminish response. Work with an ECD-experienced clinician on titration — this is an area where general-oncology dosing intuition can be wrong.

### S Side effects are manageable

Rash, joint pain, fatigue, skin sensitivity, and transient fevers are the most common. Most improve with dose adjustment or supportive medications. Photosensitivity is notable with BRAF inhibitors — sunscreen and coverage become essential.

**Work with an ECD-experienced center where possible.**

Remote consultation with MSKCC, Mayo Clinic, or another ECD center can be arranged even if your primary care happens closer to home. The ECD Global Alliance Patient Navigator will help coordinate referrals and insurance.

SECTION 06

# Open Clinical Trials (2026)

Two trials are actively recruiting ECD patients as of publication. The ECD Global Alliance Patient Navigator can match you to a trial personally — often securing trial access, free drug programs, or referral to an ECD Care Center near you. Do not navigate this alone.

**STATUS · RECRUITING**

### Mirdametinib in Histiocytic Disorders

Phase II trial. All ages (2+), all histiocytoses including ECD. MEK inhibitor with strong preclinical rationale across MAPK-driven conditions. Mirdametinib received its first FDA approval (NF1) in 2025.

`NCT06153173`

**STATUS · RECRUITING**

### Ulixertinib (ERK Inhibitor)

Phase II at Memorial Sloan Kettering Cancer Center and partner sites. Targets ERK directly — the most downstream node in the MAPK/ERK cascade. Designed for resistant or refractory disease that has progressed on upstream inhibitors.

`MSKCC & partner sites`

**Call the ECD Global Alliance Patient Navigator.**

The Navigator service — free and staffed by ECD-experienced advocates — will personally match you to trials, help with free-drug programs, and refer you to an ECD Care Center. This is the single highest-yield phone call you can make after a new diagnosis. **erdheim-chester.org**

SECTION 07

# Research & Community Timeline

From a single Viennese case report in 1930 to a targeted therapy on the formulary in 2017 — the history of ECD compressed almost a century of progress into one extraordinary decade.

| Year | Development |
|---|---|
| 1930 | First description — Jakob Erdheim and William Chester describe ECD as "lipoid granulomatosis" in Vienna. |
| 1972 | Named "Erdheim-Chester Disease" — Dr. Ronald Jaffe coins the term after reporting a similar case. |
| 2012 | BRAF V600E discovery — researchers identify recurrent BRAF V600E mutations, proving ECD is a clonal neoplasm. Targeted therapy becomes possible. |
| 2016 | WHO classification — ECD formally classified as a histiocytic neoplasm, legitimizing research funding and insurance coverage. |
| 2017 | Vemurafenib FDA approval — the first targeted therapy approved for ECD, based on the VE-BASKET trial. |
| 2019–2022 | Expanding the arsenal — MEK inhibitors (cobimetinib) show efficacy. Mayo Clinic and MSKCC publish consensus guidelines. |
| 2025 | Barcelona Gathering — ECDGA hosts Patient & Family Gathering. Mirdametinib receives first FDA approval (for NF1). |
| 2026 | Birmingham Gathering — registration open for the 2026 Patient & Family Gathering in Birmingham, Alabama. |

SECTION 08

# Voices from the Community

Four patients, four moments. These are real words from real people who became experts in a condition no one prepared them for.

> *"I spent four years being told nothing was wrong. Then another two being told they didn't know what was wrong. When I finally got the diagnosis, I wasn't relieved — I was furious. And then I got to work."*
>
> **— ECD patient · diagnosed after 6-year odyssey**

> *"The day I found the ECD community online was the first time I didn't feel like I was making this up. These people understood every scan, every setback, every small victory."*
>
> **— ECD patient and community advocate**

> *"Six months on vemurafenib and my bone pain was gone. My PET scan cleared. I went from planning my funeral to planning my daughter's graduation."*
>
> **— BRAF V600E-positive ECD patient**

> *"My oncologist had never seen a case. I printed out the consensus guidelines and brought them to every appointment. We learned together."*
>
> **— ECD patient · rural community**

**The community that exists around ECD is small but remarkably informed.**

And remarkably generous with that information. Finding the community is often the single most important thing a new patient does in the first year.

SECTION 09

# Your ECD Support Network

The organizations below exist specifically for ECD patients and families. All provide free services. Most can help navigate the logistics that make rare disease care harder than the medicine itself — insurance coding, trial enrollment, specialist referral, travel grants.

### G ECD Global Alliance — the definitive resource

Patient navigator, physician referral network, trial matching, educational webinars, annual patient & family gathering, research funding. Typically the first call for a newly diagnosed patient. **erdheim-chester.org**

### H Histiocytosis Association

Broader histiocytic disorder support that includes ECD. NCCN guidelines, clinical trial listings, NACHO (North American Consortium for Histiocytosis) access. **histio.org**

### N NORD — National Organization for Rare Disorders

Patient assistance programs, insurance navigation, and a searchable rare disease database. NORD can help with premium assistance and co-pay programs that ECD-specific organizations do not always offer. **rarediseases.org**

### F Private Facebook Groups

Search "Erdheim-Chester Disease" on Facebook. Private, moderated groups where patients share scans, side-effect strategies, and real-time support. These groups are often where the most useful day-to-day information lives.

### M MSKCC ECD Program

Memorial Sloan Kettering's dedicated ECD program. Leading clinical trials (including ulixertinib), expert consultations, and second opinions — often available remotely for patients unable to travel. **mskcc.org**

**Your story can help someone diagnosed last week.**

If you live with ECD, your experience — your mutation story, your before-and-after scans, your side-effect insights, your treatment journey — matters to the next person starting this journey. Bare Your Rare is a living resource, and your voice belongs on it.

Share your story: **bareyourrare.org/contact/**

# You Found This Place.

Bare Your Rare exists because patient experience is expertise.
This guide was built to make what took years of lived experience
and thousands of pages of literature to understand,
findable in one evening — for the person who needs it tonight.

Share it freely with your oncologist, your family,
or anyone navigating this diagnosis.

**bareyourrare.org/ecd/**

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*Grande Prairie, Alberta, Canada.*


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