



# Dr. Polyzois Makras

*251 Hellenic Airforce & VA General Hospital*

‘The LCH module: a collaboration between ERN BOND, ERN-EuroBloodNet and Endo-ERN’



**EuRREB**

European Registries for Rare  
Endocrine and Bone conditions

# The LCH module:

## a collaboration between ERN BOND, ERN-EuroBloodNet and Endo-ERN

Polyzois Makras  
Endocrinologist  
251 Hellenic Air Force & VA Gen. Hospital  
Athens, Greece

# Conflicts of interest

- Lecture fees, advisory boards: Amgen, UCB, Gilead, Galenica, Genesis, Pfizer, ELPEN, Vianex, UniPharma, Leo, Rafarm, Takeda, ITF, Ascendis, Er-Kim, Innovis Pharma, BENNETT
- Research grant : Amgen, Gilead, Galenica, ITF

Histiocytosis X

eosinophilic granuloma

Diffuse reticuloendotheliosis

Hand-Schuller-Christian disease

Letterer-Siwe disease



Langerhans Cell histiocytosis: LCH

# Langerhans Cell Histiocytosis

LCH is the most common histiocytic neoplasm that can affect children as well as adults, with incidence of approximately 5 cases/million per year in children to 1-2/million in adults, and a male to female ratio 2:1



**≈ 50%**  
**BRAF V600E**  
**mutation**

- MAPK/ERK pathway mutations

## Organ Involvement



- Bone
- Pituitary
- Skin
- Lungs
- Liver
- Lymph nodes
- CNS

## Presentation

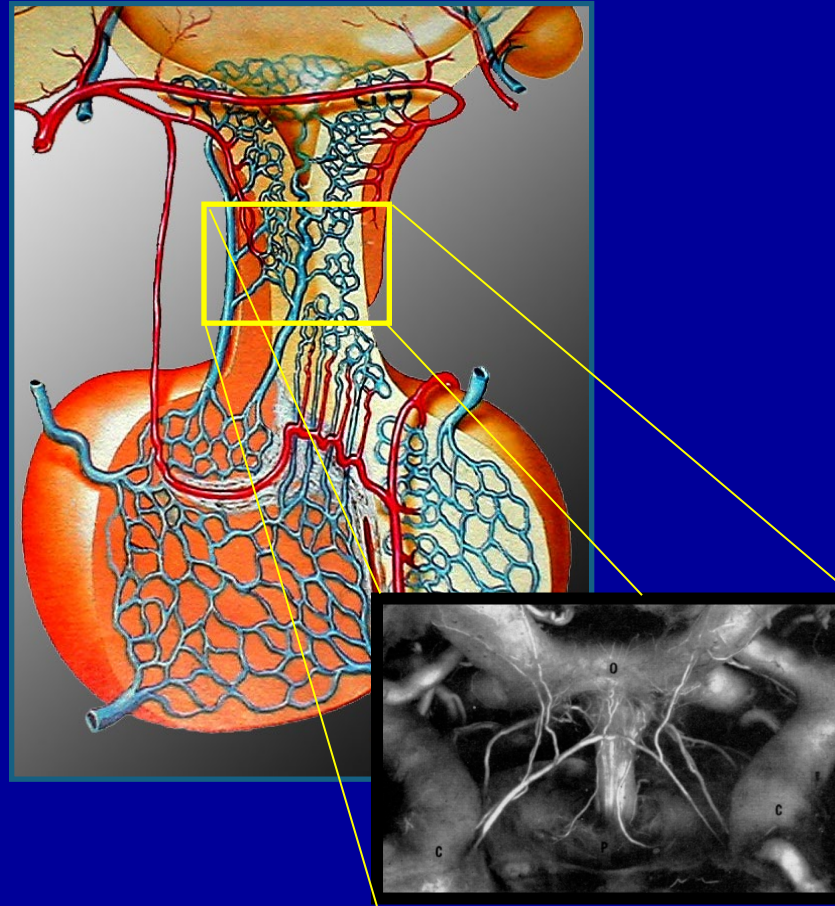


- Solitary lytic lesion
- Multisystem disease



# LCH and predilection for the Hypothalamic-Pituitary (HP) axis

- Sites of involvement
  - Hypothalamus
  - Stalk
  - Pituitary gland
- Types of involvement
  - Infiltration
  - Scarring - fibrosis
  - mass
  - Radiotherapy induced



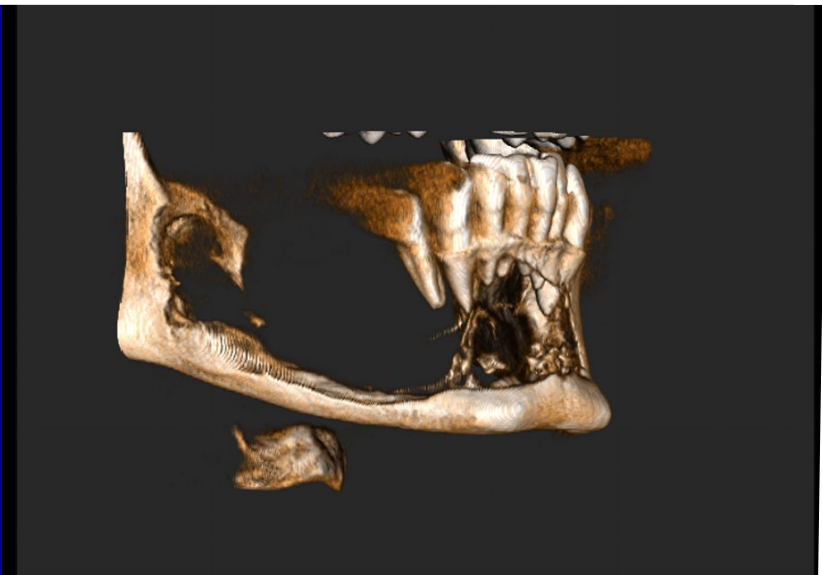
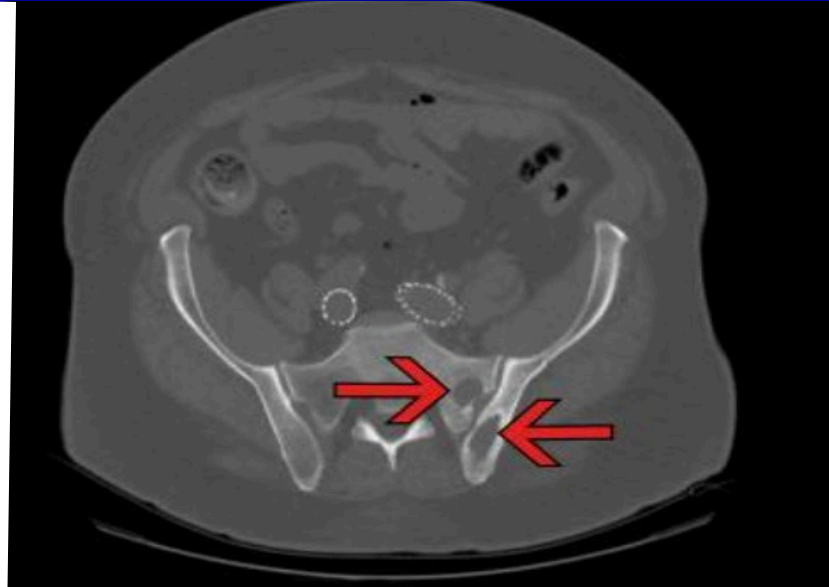
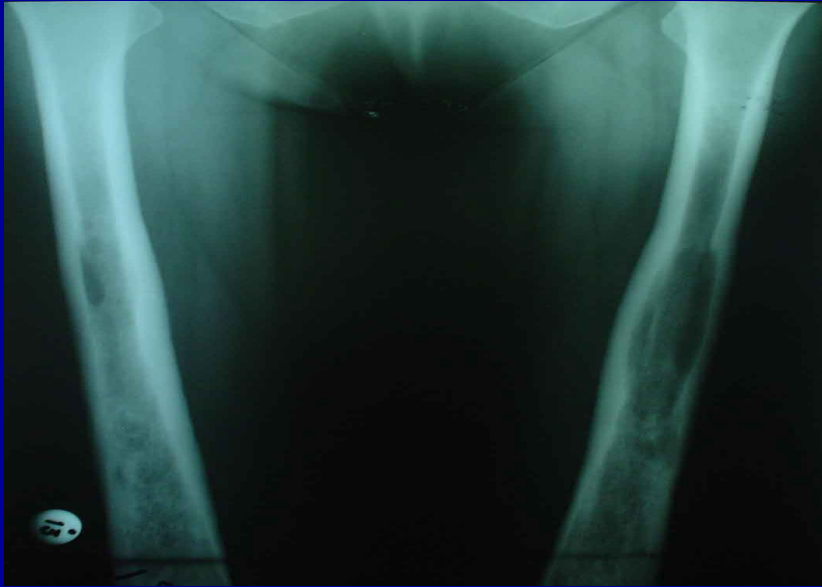
## Endocrine Involvement

- Up to 30% of patients
- AVP-D: Most common (30–60%), usually first manifestation
- Anterior Pituitary Dysfunction (APD):
  - GH deficiency (42–55%)
  - Gonadotropin deficiency (30–58%)
  - Secondary adrenal insufficiency (up to 21%)
  - Secondary hypothyroidism (~25%)
- PRL elevation in infundibular infiltration

# LCH and the skeleton

## Bone Involvement

- Most common site affected in adults
- 'Punched out' lytic lesions in skull, mandible, pelvis, mandible, ribs
- Reduced bone mineral density (20% of adults)



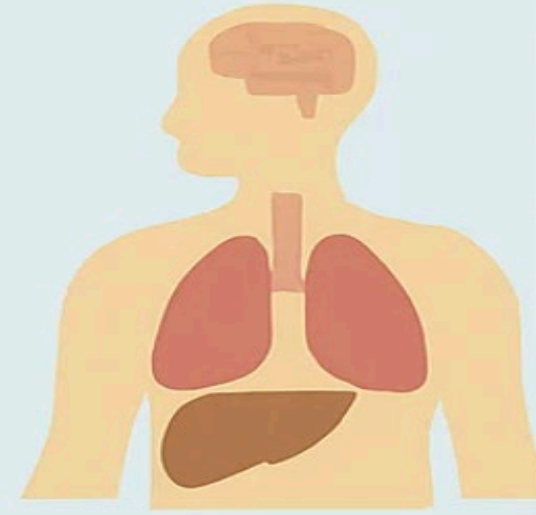
# Erdheim-Chester Disease

ECD is a rare histiocytic neoplasm biologically similar to LCH, with BRAF V600E and other MAPK/ERK mutations. ECD primarily affects middle-aged to older adults with a male preponderance. The incidence of ECD is unknown as it was recently recognized as a hematopoietic neoplasm, but approximately 1,500 cases have been reported to date.



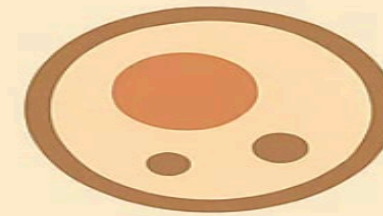
**≈ 50 %  
BRAF V600E  
mutation**

## Organ Involvement



- Bone
- CNS
- Pituitary
- Kidney
- Lungs
- Aorta
- Retroperitoneum

## Presentation



- Multisystem disease
- Bilateral osteosclerosis of long bones



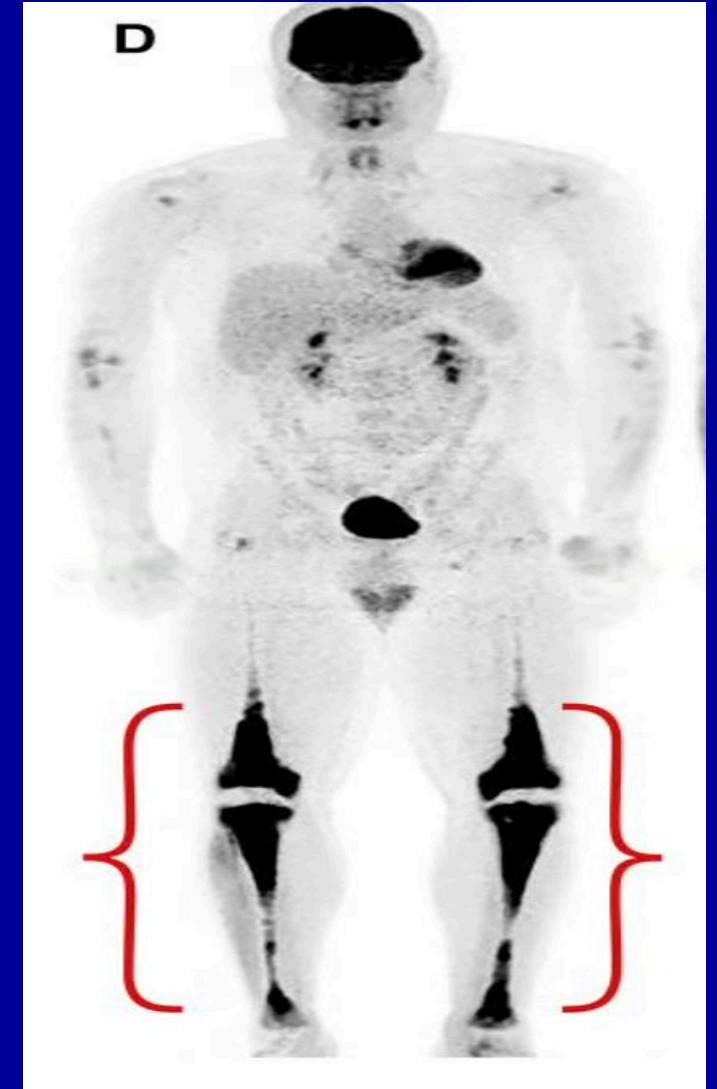
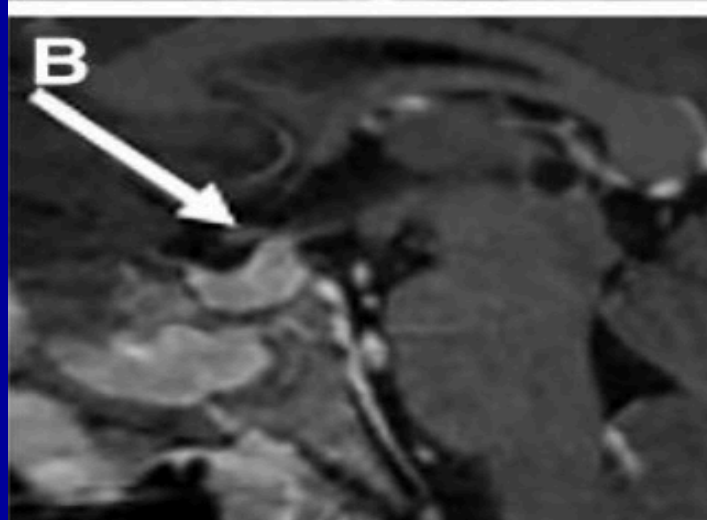
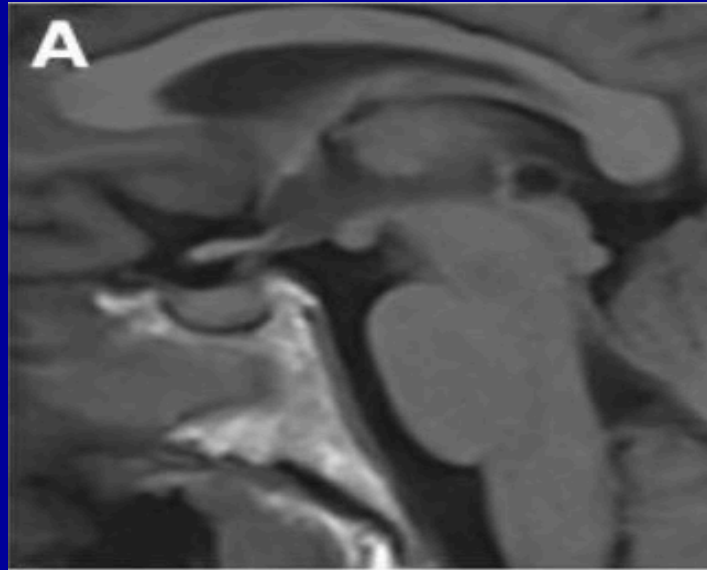
# Endocrine and skeletal manifestations in ECD

## Endocrine Involvement

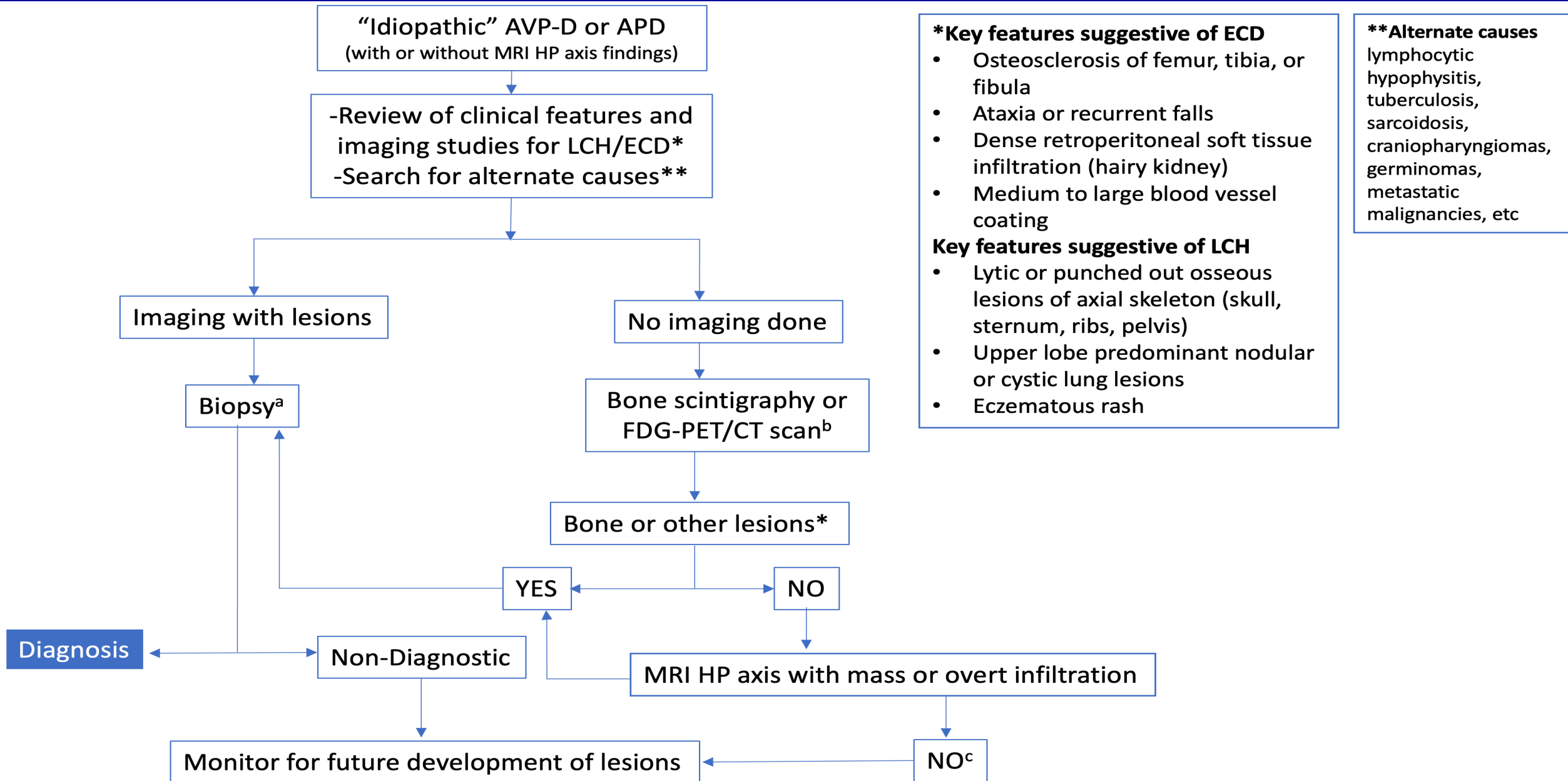


In nearly 50-60% of cases

- AVP-D in 29-33%
- Growth hormone deficiency in 78%



# From endocrinopathy to the diagnosis of a histiocytic disorder



# How to add a new patient

Click on “Add” from the menu tab “Patients”



Fill in all mandatory fields in the Common Data Elements, choose test patient box and “SYSTEMIC & RHEUMATOLOGICAL” to use the LCH module

**Add Patient**

☒ Is Test Case ?

Fields marked with \* are mandatory

\* Consent for Core Registry ☐ Opt-in ? ☐ Opt-out ?

\* Date of Birth ?

\* Condition Group (select all that apply)

☐ ADRENAL ? ☐ CALCIUM & PHOSPHATE ? ☐ GLUCOSE & INSULIN ?

☐ GENETIC ENDOCRINE TUMOURS ? ☐ GROWTH & OBESITY ? ☐ HYPOTHAL & PITUITARY ?

☐ SEX DEVELOPMENT ? ☐ THYROID ? ☐ BONE DYSPLASIA ?

☒ SYSTEMIC & RHEUMATOLOGICAL ?

Pseudonymised ID (e.g. SPIDER)

\* Sex at Birth ☐ Male ☐ Female ☐ Other ☐ Unknown

Current Gender ☐ Male ☐ Female ☐ Non-binary ☐ Other ☐ Asked but unknown

\* Country of Birth

\* Country of Usual Residence

\* Patient Follow-up Status ☐ Patient active ☐ Patient inactive ☐ Patient care suspended ☐ Patient care terminated ☐ Deceased ☐ Unknown

**Save and continue** **Cancel**



# Fill in the mandatory fields in the condition group section

1

Edit To Do

Core Data

SYSTEMIC & RHEUMATOLOGICAL

Generic Outcomes

Diagnosis-specific Outcomes

Documents

Audit

Patient List

Systemic & Rheumatological

Senior Clinician < 18 - N/A

Senior Clinician ≥ 18 - N/A

e-REC ID ?

\* First Contact with Centre ?

2024-06-01

\* Clinician Responsible for Patient ?

Mariya Cherenko

\* Date of First Clinical Manifestations ?

2024-05-09

\* Primary Condition

Multisystem Langerhans cell histiocytosis

\* Specific Diagnosis

The full hierarchy of Conditions and Specific Diagnoses can be found in the [Core Registry C](#)

- Select -

Langerhans cell histiocytosis, unifocal

Langerhans cell histiocytosis, single-system multifocal

Pulmonary Langerhans cell histiocytosis

Multisystem Langerhans cell histiocytosis

How Was Diagnosis Reached ?

☐ MRI ☐

\* Date of Diagnosis ?

Participation in another Detailed Disease Registry

Save



# Fill in the mandatory fields in the condition group section

1

Edit To Do

Core Data

SYSTEMIC & RHEUMATOLOGICAL

Generic Outcomes

Diagnosis-specific Outcomes

Documents

Audit

Patient List

Systemic & Rheumatological

Senior Clinician < 18 - N/A

Senior Clinician ≥ 18 - N/A

e-REC ID ?

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\* Clinician Responsible for Patient ?

Mariya Cherenko

\* Date of First Clinical Manifestations ?

2024-05-09

\* Primary Condition

Non-Langerhans cell histiocytosis

\* Specific Diagnosis

Erdheim-Chester disease

- Select -

Non-Langerhans cell histiocytosis

Erdheim-Chester disease

Rosai-Dorfman disease

The full hierarchy of Conditions and Specific Diagnoses can be found in the [Core Registry C](#)

How Was Diagnosis Reached ?

☐ MRI ☐

\* Date of Diagnosis ?

Participation in another Detailed Disease Registry

☐ Yes ☐ No ☐ Not known

Save

# Access for a patient to the Core Registry

If your patient consented for the access to the Core Registry:

\* Can be contacted for research purposes by clinician responsible for patient ☒ Yes ☐ No ☐ Not Known

\* Data can be shared for research purposes ☒ Yes ☐ No ☐ Not Known

Can be contacted for collecting Patient Reported Outcomes ☐ Yes ☐ No ☒ Not Known

\* Patient would like access to Core Registry ☒ Yes ☐ No ☐ Not Known

Consent for Newsletters ☐ Yes ☐ No ☒ Not Known

After ticking the correspondent answer, 'Patient Access' button will appear automatically in the menu

Core Data **SYSTEMIC & RHEUMATOLOGICAL** Patient Access Generic Outcomes Diagnosis-specific Outcomes

Documents Audit Patient List

Core Data SYSTEMIC & RHEUMATOLOGICAL Patient Access Generic Outcomes Diagnosis-specific Outcomes Documents Audit Patient List

This is a preview of the data the Patient will see if you approve this access. The Patient will also have the facility to change consents and to request data deletion.

Patient Core SYSTEMIC & RHEUMATOLOGICAL Centre	
Patient Registry ID	7474
Consent Type for Registry	Opt-in
Date added to Registry	2025-03-26
Date of Birth	1969-09-24
Pseudonymised ID (e.g. SPIDER)	
Sex at Birth	Female
Current Gender	
Country of Birth	NETHERLANDS
Country of Usual Residence	NETHERLANDS
Patient Follow-up Status	Patient active

Enter the Patient's Email Address, edit your default Patient Invitation Message if required and click on Grant Access to approve access to this data. The patient will need to enter a Date of Birth that matches the one entered by you in this Registry to successfully activate the account. If you didn't enter the actual date of birth, please provide this information in the invitation below.

\* Patient Email

Additional Message to Patient




Patient Preferred Language - Select -

Grant Access

You need to know your patient's e-mail address. The system will send the invitation link. You can write an additional message and choose preferred language. On the platform patient can see the information about him/her and fill in the PROMs.



# Fill in patient's data

Basic module		Treatment	Malignancies and Comorbidities
Assessment Date		<input type="text" value="yyyy-mm-dd"/> 	
Race	<div>- Select -</div>		
Disease activity	<input type="radio"/> Active <input type="radio"/> Inactive		
Diagnostic specimen site (biopsy)	<div><input type="checkbox"/> Skin</div> <div><input type="checkbox"/> Bone</div> <div><input type="checkbox"/> Bone marrow</div> <div><input type="checkbox"/> Lymph node</div> <div><input type="checkbox"/> Lung (Bronchoalveolar lavage)</div> <div><input type="checkbox"/> Lung</div> <div><input type="checkbox"/> CNS</div> <div><input type="checkbox"/> Liver</div> <div><input type="checkbox"/> Kidney</div> <div><input type="checkbox"/> Abdominal cavity</div> <div><input type="checkbox"/> Other</div>		
BRAF testing	<div><input type="radio"/> BRAF V600e (+)</div> <div><input type="radio"/> BRAF V600e (-)</div> <div><input type="radio"/> Non -V600e BRAF (+)</div> <div><input type="radio"/> Not performed</div>		
Other mutations	<div><input type="radio"/> MAP2K</div> <div><input type="radio"/> NRAS</div> <div><input type="radio"/> KRAS</div> <div><input type="radio"/> Other</div> <div><input type="radio"/> Not performed</div>		
Organs involved		<div><input type="checkbox"/> Bone</div> <div><input type="checkbox"/> Pituitary</div> <div><input type="checkbox"/> Endocrine non pituitary</div> <div><input type="checkbox"/> Lymph nodes</div> <div><input type="checkbox"/> Marrow</div> <div><input type="checkbox"/> Skin</div> <div><input type="checkbox"/> Soft tissue</div> <div><input type="checkbox"/> Liver</div> <div><input type="checkbox"/> Spleen</div> <div><input type="checkbox"/> Ocular</div> <div><input type="checkbox"/> Meninges</div> <div><input type="checkbox"/> CNS</div> <div><input type="checkbox"/> Sinus</div> <div><input type="checkbox"/> Cardiovascular</div> <div><input type="checkbox"/> Kidneys</div> <div><input type="checkbox"/> Retroperitoneal</div> <div><input type="checkbox"/> Oral mucosa</div> <div><input type="checkbox"/> Genitalia</div> <div><input type="checkbox"/> Other</div>	

# Fill in patient's data

Basic module	Treatment	Malignancies and Comorbidities
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Current treatment	<input type="radio"/> Not Known <input type="radio"/> Yes <input type="radio"/> No
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Lines of treatment in the past	<input type="radio"/> Cladribine based
	<input type="radio"/> Cytarabine based
	<input type="radio"/> Other systemic chemotherapies
	<input type="radio"/> Radiotherapy with or without steroids
	<input type="radio"/> Resection
	<input type="radio"/> Systemic steroids
	<input type="radio"/> Local steroids
	<input checked="" type="checkbox"/> Targeted treatment
	<input type="radio"/> Bisphosphonates
	<input type="radio"/> Denosumab
	<input type="radio"/> Methotrexate
	<input type="radio"/> Azathioprine/6-mercaptopurine
	<input type="radio"/> Immunomodulatory drugs
	<input type="radio"/> Other

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Type of targeted treatment in the past	<input type="radio"/> Vemurafenib
	<input type="radio"/> Dabrafenib
	<input type="radio"/> Cobimetinib
	<input type="radio"/> Trametinib
	<input type="radio"/> Binimetinib
	<input type="radio"/> Pexidartinib
	<input type="radio"/> Sorafenib
	<input type="radio"/> Dabrafenib and trametinib
	<input type="radio"/> Other



# Fill in patient's data

Basic module		Treatment		Malignancies and Comorbidities	
Assessment Date		<div>?</div>		<div>2025-05-06</div> <div></div>	
Other malignancies?		<div><div></div> Not Known</div> <div><div></div> Yes</div> <div><div></div> No</div>			
Type of other malignancies		<div><div></div> Carcinoma</div> <div><div></div> Sarcoma</div> <div><div></div> Myeloma</div> <div><div></div> Leukemia</div> <div><div></div> Lymphoma</div> <div><div></div> Mixed types</div> <div><div></div> Other</div>			
Comments regarding malignancies		<div></div>			
Comorbidities not directly related to ECD		<div><div></div> Not Known</div> <div><div></div> Yes</div> <div><div></div> No</div>			
Types of comorbidities		<div><div></div> Cardiovascular disease</div> <div><div></div> Diabetes</div> <div><div></div> Hypelipidemia</div> <div><div></div> Autoimmune disorders</div> <div><div></div> Chronic respiratory diseases</div> <div><div></div> Allergies</div> <div><div></div> Obesity</div> <div><div></div> Neurological diseases</div> <div><div></div> Substance abuse</div> <div><div></div> Infectious diseases</div> <div><div></div> Mental illness</div> <div><div></div> Osteoporosis</div>			
		<div><div></div> Bone disease</div> <div><div></div> Other</div>			
Comments for comorbidities		<div></div>			

Thank you for your  
attention!

pmakras@gmail.com  
info@adulch.gr

# Acknowledgements



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## CSM Development Group

Natasha Appelman-Dijkstra, LUMC, The Netherlands  
Maria Yavropoulou, LAIKO Hospital, Greece  
Antonis Kattamis, Agia Sophia Hospital, Greece  
Jan A.M. van Laar, Erasmus MC, The Netherlands  
Daniel El Fassi, Copenhagen Univ. Hospital, Denmark  
  
Histiocytosis Hellas, Patients' Association, Athens Greece  
  
Mariya Cherenko, LUMC, The Netherlands  
Tess de Rooij, LUMC, The Netherlands

# Thank you

## Ways to contact us:



[eurreb.eu](http://eurreb.eu)



[registries@lumc.nl](mailto:registries@lumc.nl)



drop-in sessions via Zoom



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