

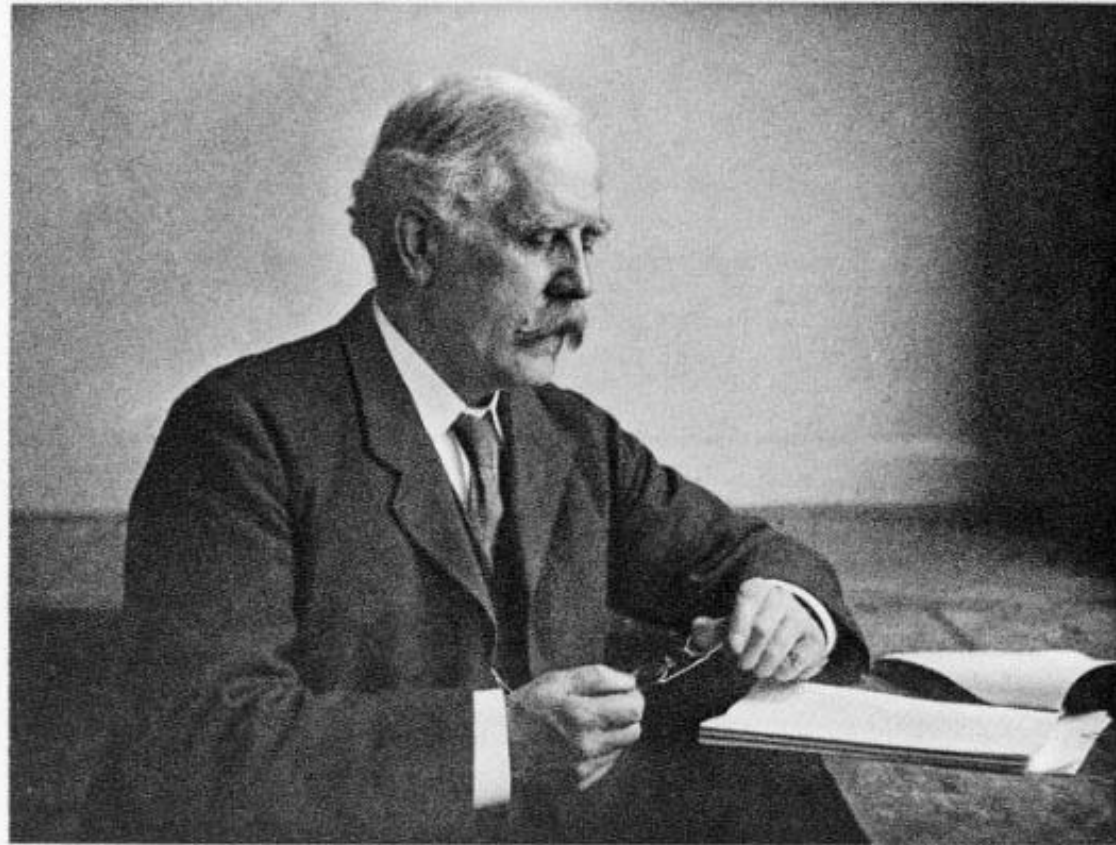
# The patients' perspective on the value of orphan designation - the case of the AKU Society

Dr Nicolas Sireau,  
Chair & CEO, AKU Society  
[nick@akusociety.org](mailto:nick@akusociety.org)



# About Alkaptonuria (AKU)

# 1902: Sir Archibald Garrod



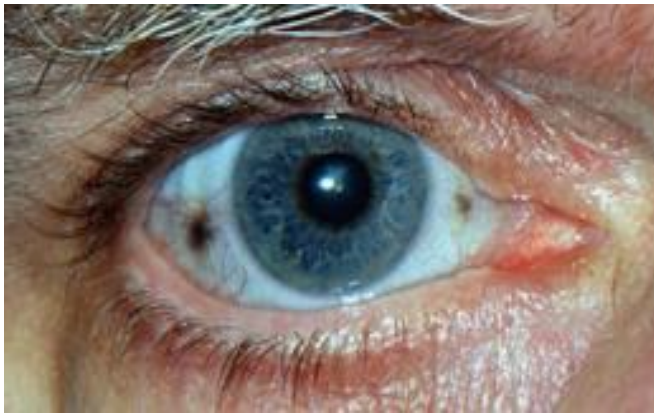
*A. Garrod.*

# Harwa

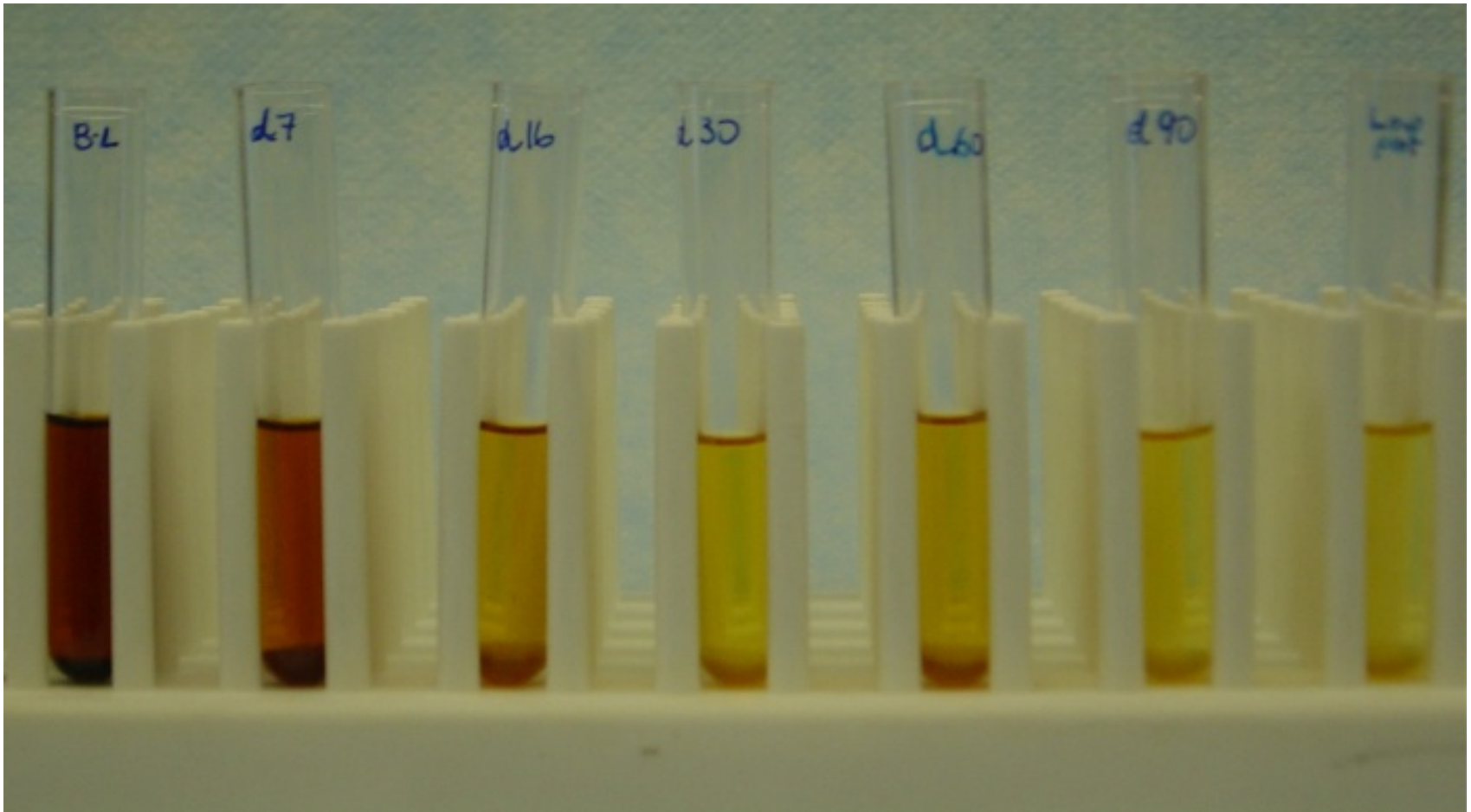
Oldest AKU Patient 1500 BC



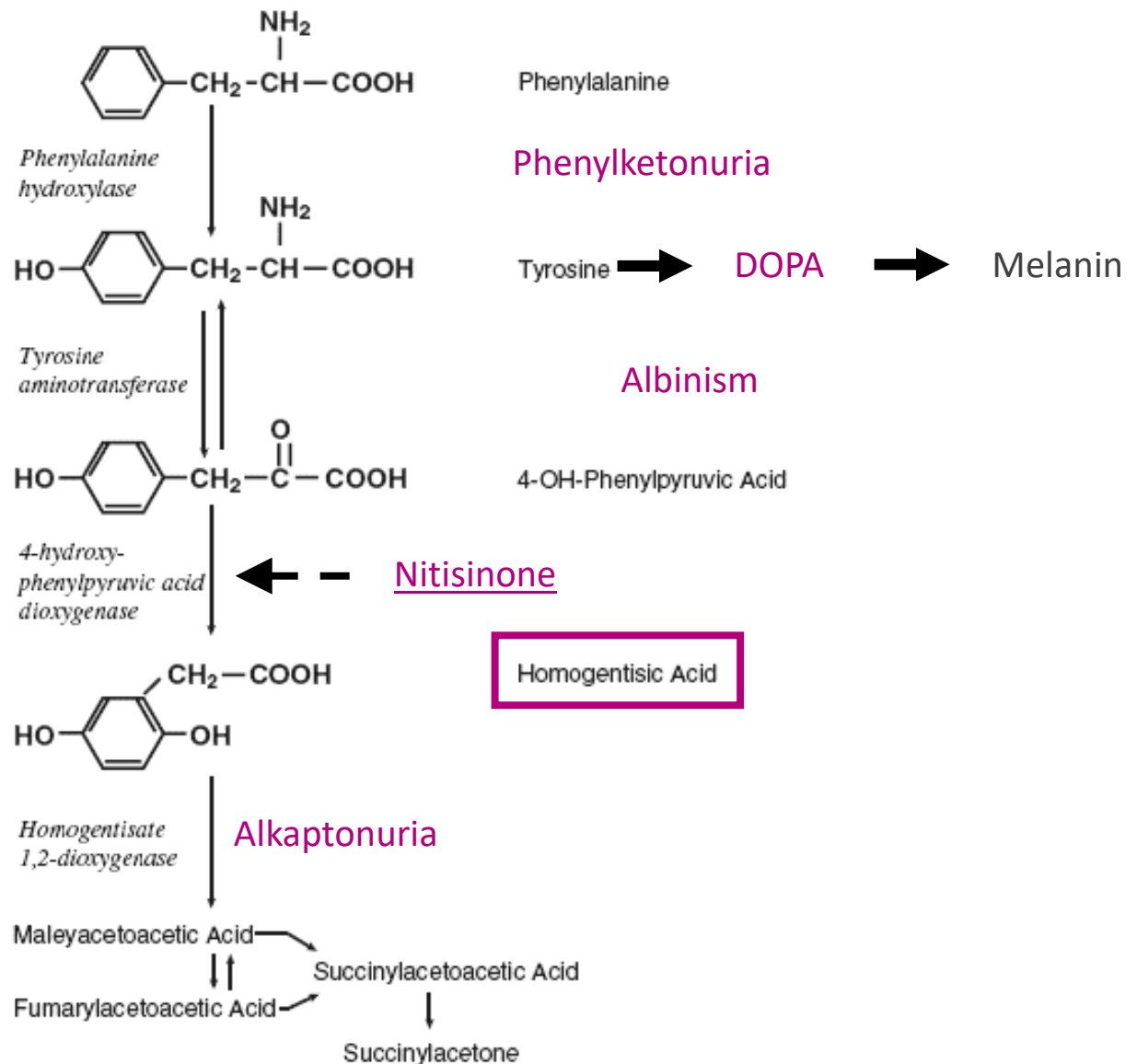
# The AKU Tetrad



# Urinary HGA



# Metabolic Pathway



Tyrosinaemia Type 1

# The value of orphan designation





The European Agency for the Evaluation of Medicinal Products  
*Pre-authorisation Evaluation of Medicines for Human Use*

London, 6 January 2003  
EMA/COMP/140/02 Rev. 1

**COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS**

**PUBLIC SUMMARY OF  
POSITIVE OPINION FOR ORPHAN DESIGNATION  
OF  
nitisinone  
for the treatment of alkaptonuria**

On 13 March 2002, orphan designation (EU/3/02/096) was granted by the European Commission to Swedish Orphan International AB, Sweden, for nitisinone for the treatment of alkaptonuria.

**What is alkaptonuria?**

Alkaptonuria is a genetic disease, where a deficiency in an enzyme, the homogentisic acid oxidase, leads to the accumulation of homogentisic acid (HGA) and its metabolites, which have deleterious effects on cartilage. The condition is sometimes revealed in infants by a bluish colour of eye conjunctiva, or dark colouring of urine in diapers. The most common symptoms occur during

# How orphan designation enabled us to carry out clinical trials

# Three Studies

Trial Name	Description	Sites
<b>SONIA 1:</b> Suitability of Nitisinone in Alkaptonuria 1	3-month phase II study	UK/Slovakia
<b>SONIA 2:</b> Suitability of Nitisinone in Alkaptonuria 2	4-year phase III	UK/Slovakia/France
<b>SOFIA:</b> Subclinical Ochronosis Features in Alkaptonuria	Cross-sectional study	UK

# Develop AKUre

The Royal Liverpool and Broadgreen University Hospitals   
NHS Trust

Hôpital Necker  
Enfants Malades



Clinical Sites

Regulatory & Monitoring



# Consortium

# AKU

+ Alkaptonuria Society →



Patient Support

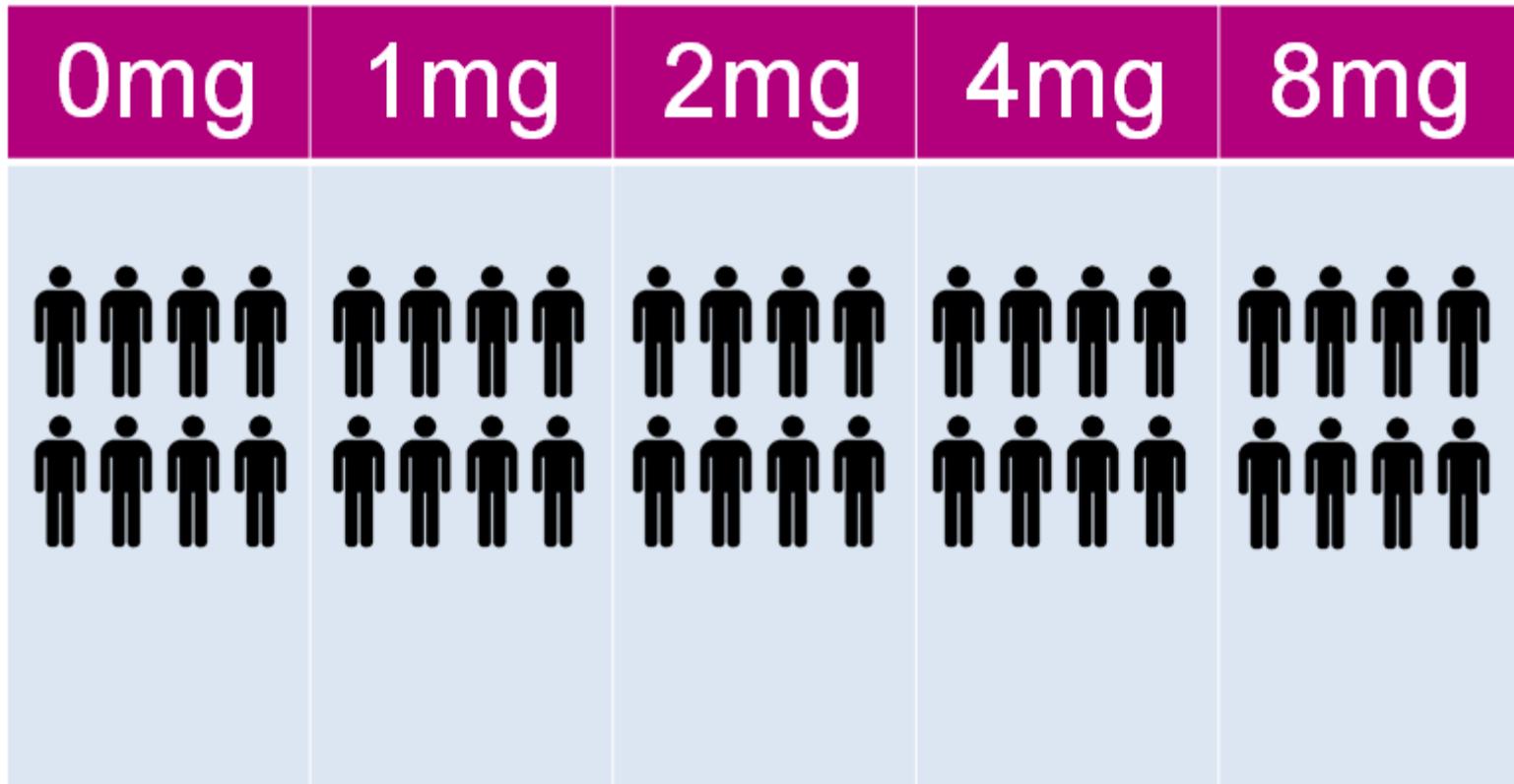
Analysis



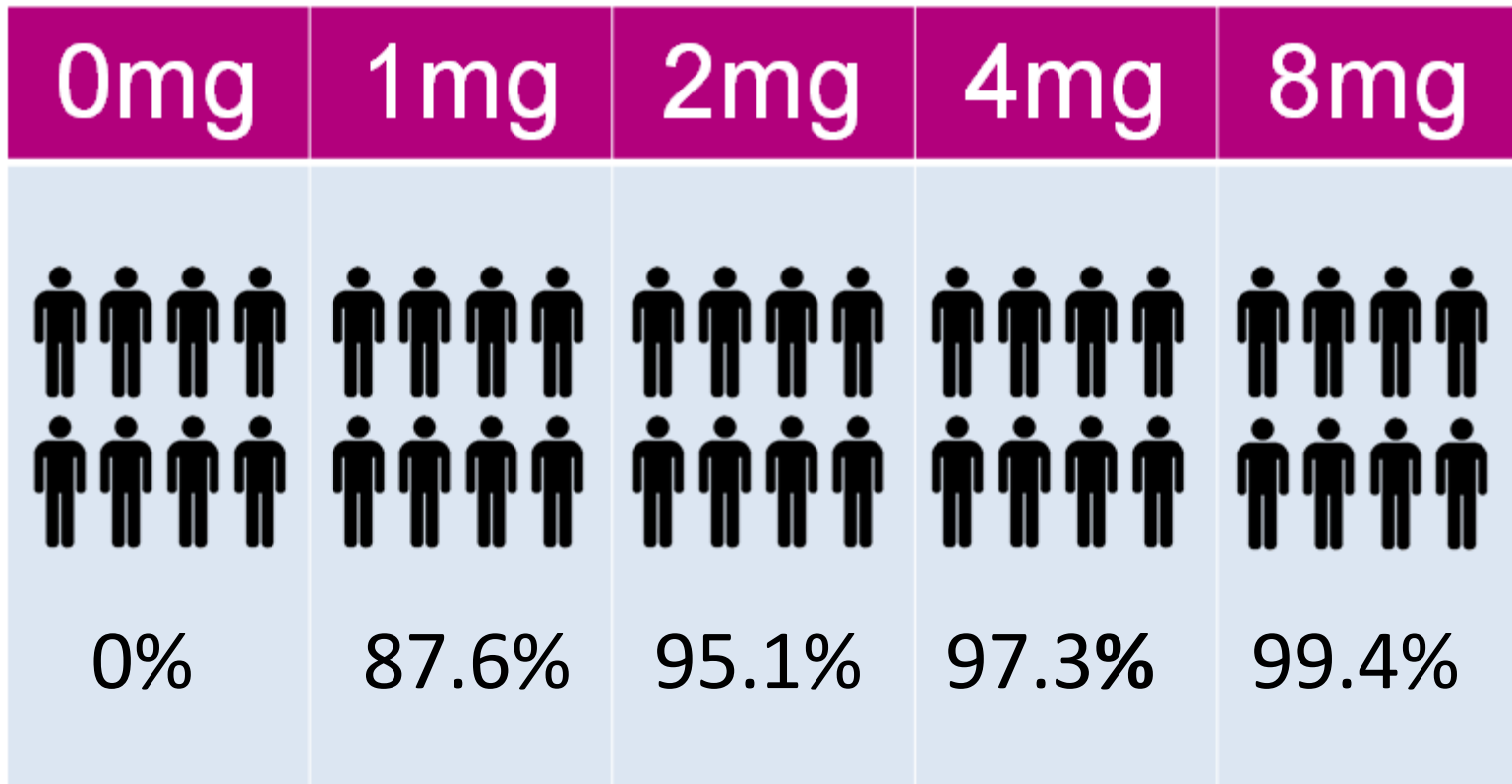
How Patients Can Lead  
Drug Development



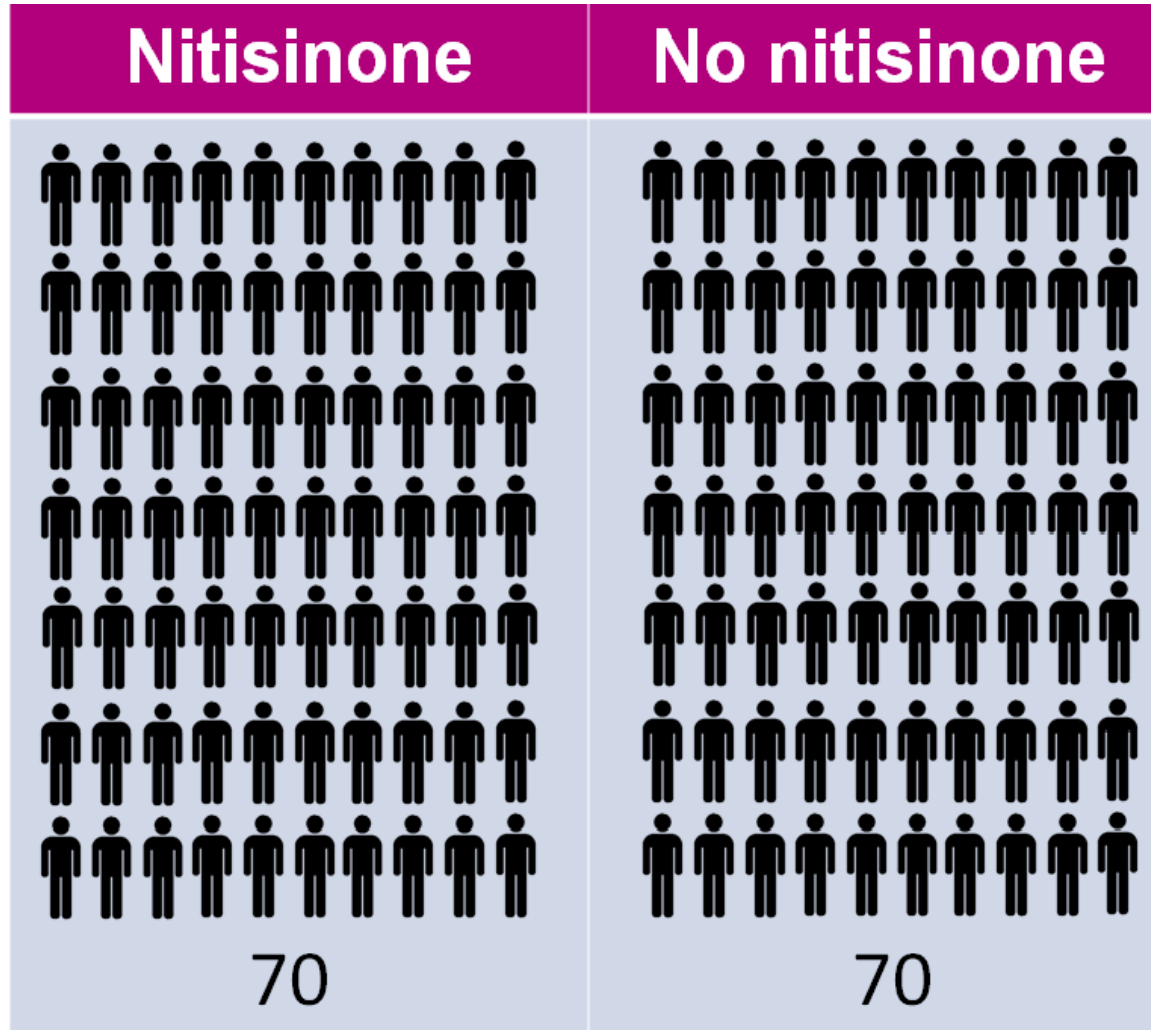
# SONIA 1



# SONIA 1



# SONIA 2





# Clinical Sites

1

## At Liverpool, UK

The Royal Liverpool University Hospital, UK, is home to the National AKU Centre, and some of the world's leading experts on the disease.  
*Lead clinician – Prof L Ranganath*

2

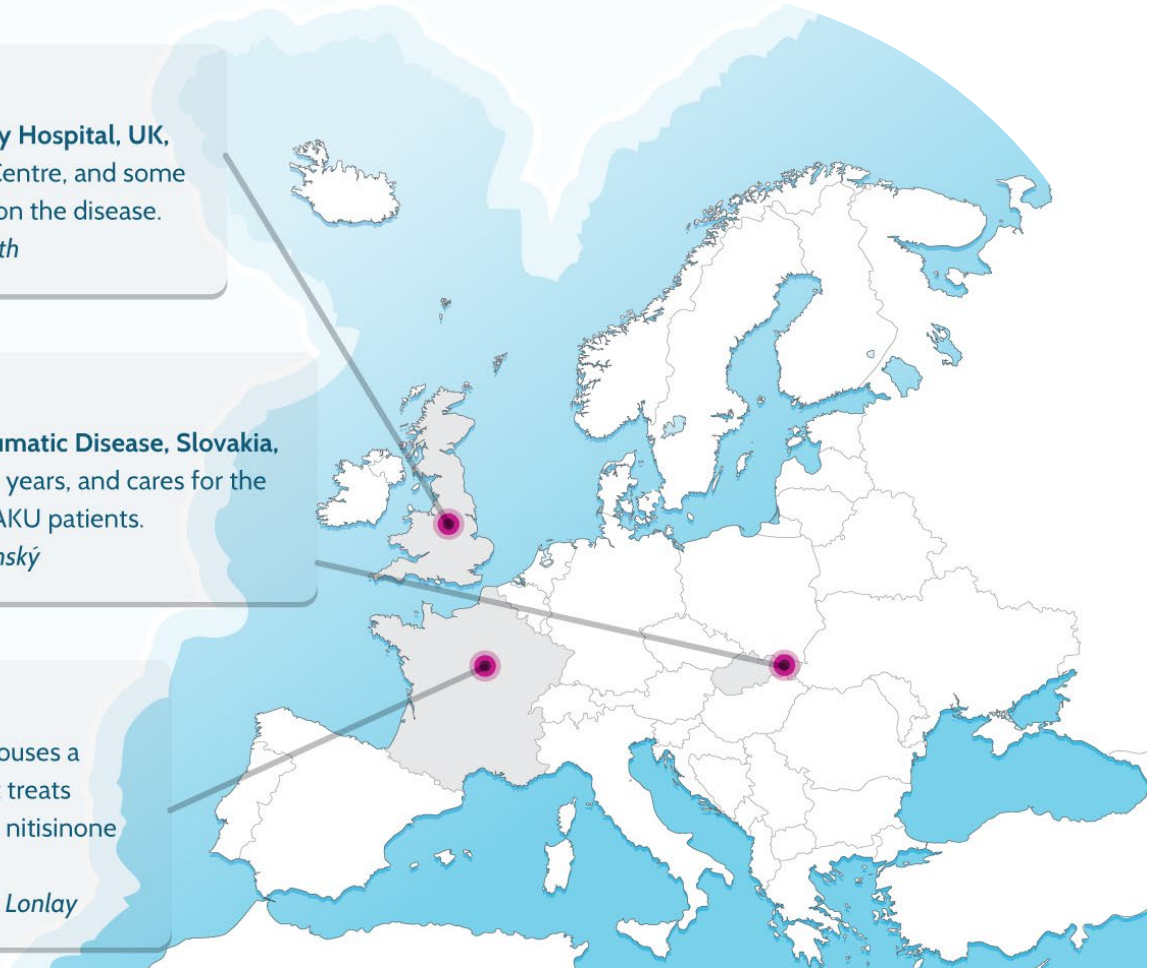
## At Piestany, Slovakia

The National Institute of Rheumatic Disease, Slovakia, has been studying AKU for 60 years, and cares for the world's largest community of AKU patients.  
*Lead clinician – Prof Jozef Rovenský*









3

## At Paris, France

The Hôpital Necker, France, houses a national metabolic centre that treats several AKU patients and uses nitisinone for tyrosinaemia patients.  
*Lead clinician – Prof Pascale de Lonlay*



# SOFIA

	M / F		M / F
16-20		36-40	
21-25		41-45	
26-30		45-50	
31-35		50+	

Statistical significance reached!

EMA provides positive opinion!

EC grants marketing authorization!

# Challenges and opportunities

# Challenges and opportunities

- Funding obstacles
- End point questions
- Working with pharma
- Setting up a consortium
- Identifying and recruiting rare disease patients

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