



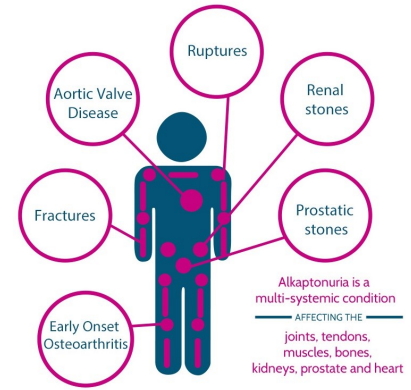
The first effective treatment for AKU: A collaborative, patient centric effort

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What is alkaptonuria (AKU)?

Alkaptonuria, also known as AKU or Black Bone Disease, is an extremely rare genetic condition, which can cause significant damage to the bones, cartilage and tissues of those affected. AKU normally only affects one in every 250,000 people worldwide. AKU is a recessive condition that is caused by a mutation of one chromosome, this means that if two people carry the faulty gene, their child still only has a 25% chance of developing AKU.

AKU stops patients' bodies from breaking down a chemical called homogentisic acid (HGA) which the body naturally produces during the digestion of food. Due to this, HGA builds up in the body and, over time, leads to black and brittle bones and cartilage, and early onset osteoarthritis. The build up of HGA in the body can also lead to other, sometimes more serious health complications.



"It feels as if your bones are wrapped in barbed wire" - AKU Patient

DevelopAKUre

The DevelopAKUre programme was a series of three major international clinical trials run by a consortium of 13 European partners. It aimed to study a new drug, called nitisinone, and assess its effectiveness in treating AKU. Nitisinone is not currently licensed for AKU but is being used by many patients off-label and at the National Alkaptonuria Centre in Liverpool. Those patients experience benefit, but the only way to be sure a drug works is through clinical research. We recruited 138 patients from all over Europe to take part, with trial sites in Liverpool, UK, Paris, France, and Piešťany, Slovakia.

In July 2019, we found out that the trials were successful and showed a reduction in the acid that causes AKU. Due to this, SOBI (Swedish Orphan Biovitrum) will apply to get the drug licensed as a treatment for AKU at the European Medicines Agency (EMA).

The project involved a dose-response study SONIA 1 (Suitability of Nitisinone In Alkaptonuria 1), an efficacy study SONIA 2 (Suitability of Nitisinone In Alkaptonuria 2) to compare no-treatment to treatment, and a cross-sectional study SOFIA (Subclinical Ochronotic Features in Alkaptonuria) to determine the best age to begin treatment. DevelopAKUre was patient-led, with the AKU Society as a lead partner, ensuring patient views were considered at planning stages, and throughout the studies. The AKU Society led on patient recruitment and support, developing patient information documents and ensuring very high patient retention.

Patients' needs were taken into consideration in the design of the trial. This included reducing the amount of time participants spent in each of the trial sites. Based on feedback from SONIA 1, we explained to other stakeholders the importance of patients having 'downtime' and not staying in hospital as if they were ill. Due to this, for the second stage of the project's clinical trial, patients stayed in a nearby hotel. Feedback from this move was overwhelmingly positive and led to patients from across Europe seeing their visit as a holiday.

It was also noted that due to the nature of the disease, patients might have severe mobility issues. As a reflection of this, and with feedback from the patient group, it was decided that those patients would be accompanied by a chaperone who was fully reimbursed. Normally this was a family member who acted as a carer. This was vital, as patients communicated, they would not come without one and allowed for continuity of care.

Recruitment was efficient because patients were helping in the discussions as well as finding patients outside of our network. Patients understood the benefit of the trials for themselves and the patient community. This was shown to them with reference to existing research and by a simple and accessible explanation on the trials' website.

We see a future where nitisinone is licensed all over the world as a treatment for AKU, a future where children with AKU will grow up with none of the damaging symptoms of the disease. We are now closer to this reality.

Paris, France
Piešťany, Slovakia.
Liverpool, UK



The Royal Liverpool and Broadgreen University Hospitals
NHS Trust