Statutory Approvals Committee – minutes

Centre 0101 (CARE Nottingham)

Pre-implantation Genetic Diagnosis (PGD) application for Alexander Disease (ALX), OMIM #203450

Thursday, 26 September 2019

HFEA, Spey Meeting Room, Level 2, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Anne Lampe Emma Cave Ruth Wilde	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Dr. Jenny Carmichael	
Legal Adviser	Tom Rider	FieldFisher LLP
Observer	Bernice Ash	Committee Officer

Declarations of interest

- Members of the committee declared that they had no conflicts of interest in relation to this item.

The committee had before it:

- 9th edition of the HFEA Code of Practice.
- Standard licensing and approvals pack for committee members.

The following papers were considered by the committee:

- Executive Summary
- PGD Application Form
- Redacted Peer Review for ALX
- Redacted Peer Review for two further similar leukodystrophies – Salla Disease & Refsum Disease
- Genetic Alliance UK statement
- Statutory Approvals Committee Minutes, 25 April 2019 – PGD for Multiple Sulfatase Deficiency
- Licence Committee Minutes, 1 March 2012 - PGD for Hydroxyglutaric Aciduria
- Licence Committee Minutes, 26 January 2012 - PGD for Canavan Disease
- Licence Committee Minutes, 5 May 2011 - PGD for CADASIL

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Jenny Carmichael, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for Alexander Disease (ALX), OMIM # 203450 is consistent with the peer review.

1.3. The committee noted that the condition being applied for is not on the list of approved PGD conditions.

1.4. The committee noted that the Genetic Alliance UK statement provided a perspective on the impact of the condition on patients, their families and carers.

1.5. The committee had regard to its decision tree. The committee noted that the centre is licensed to carry out PGD. The committee was also satisfied that the centre has experience of carrying out PGD and that generic patient information about its PGD programme and associated consent forms had previously been received by the HFEA.

1.6. The committee noted that the proposed purpose of testing the embryos was as set out in paragraph 1ZA(1)(b) of Schedule 2 of the Act, i.e. 'where there is a particular risk that the embryo may have any gene, chromosome or mitochondrion abnormality, establishing whether it has that abnormality or any other gene, chromosome or mitochondrion abnormality'.

1.7. The committee noted that Alexander Disease (ALX), OMIM #203450, is inherited in an autosomal dominant pattern, which means there is a 50% chance of an embryo being affected by the condition in each pregnancy if either parent has a relevant mutation.

1.8. The committee noted the penetrance of the condition is 100%.

1.9. ALX is a collection of symptoms caused by the destruction of myelin. The earlier the symptoms develop, the worse the condition and the prognosis. The condition can be present from birth and although the neonatal form of ALX is rare, it is associated with severe intellectual developmental delay, a build-up of fluid in the brain, seizures and death in infancy. The infantile form of ALX is the most prevalent form and is diagnosed before 2 years of age, with severe developmental delay, abnormal physiology and death by the age of 10 years. The juvenile form is less common and the adult form is rare but both lead to developmental regression and loss of motor control.

1.10. There is no cure or treatments for this condition which can result in early death.

1.11. The committee noted the executive's request to consider Alexander Disease (ALX), OMIM #203450 for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.12. The committee noted that at the request of the executive, the peer reviewer had agreed that two other conditions had a comparable phenotype to ALX. These were Refsum Disease, OMIM #266500 and Salla Disease, OMIM #604369. Salla disease is a neurodegenerative disorder, which may also present as a severe infantile form, known as Infantile Sialic Acid Storage Disorder (ISSD), OMIM #269920.

2. Decision

2.1. The committee considered that, in the worst-case scenario Alexander Disease (ALX), OMIM #203450 is a devastating and progressive disease that can present in childhood. There is no cure or treatment options to mitigate the condition which can lead to early death. Most patients with either the neonatal form or the infantile form die within 10 years of onset.

2.2. The committee considered that in the worst-case scenario, Salla Disease, OMIM # 604369, and Infantile Sialic Acid Storage Disorder (ISSD), OMIM #269920, are devastating neurodegenerative conditions of similar severity and clinical presentation to Alexander Disease (ALX) OMIM #203450. There is no cure for the conditions which present during the neonatal period or in infancy. The conditions are both life-limiting with death occurring in early childhood.

2.3. Regarding Refsum Disease OMIM #266500, the committee welcomed the advice of the specialist adviser and agreed that as this condition was of a different phenotype, it was not appropriate to consider it under this application.

2.4. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormalities in question and that there is a significant risk, that a person with such an abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

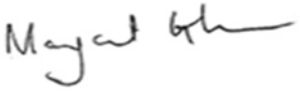
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Alexander Disease (ALX), OMIM #203450
- Salla Disease, OMIM #604369
- Sialic Acid Storage Disorder (ISSD), OMIM #269920

3. Chairs signature

3.1. I confirm this is a true and accurate record of the meeting,

Signature



Name
Margaret Gilmore

Date
28 October 2019